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OCCLUSION OF THE BASILAR ARTERY—A CLINICAL AND PATHOLOGICAL STUDY.

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AT the outset we wish to state that it is not intended to include in this article an account of all the diverse brain-stem syndromes which may follow occlusion of the branches of the basilar artery. These have been discussed in numerous publications and are well known to neurologists under such eponyms as the syndrome of Millard-Gubler, Foville, Weber, Benedict and others. Instead, it is our purpose to discuss the symptomatology and pathology of occlusion by thrombosis and embolism of the basilar artery itself. We believe that pertinent facts and observations have come into our possession which permit some clarification of a heretofore obscure clinical syndrome and also cast some light on the phenomenon of acute decerebration in man.

The report is based on the study of 18 cases, some of which were examined by us during life, and all of which were submitted to autopsy. The cases were gathered from the records of the Department of Pathology at the Massachusetts General Hospital and the Mallory Institute of Pathology at Boston City Hospital. In all we have found 13 cases among 4,200 consecutive autopsies at the Massachusetts General Hospital and 12 cases among the last 3,200 autopsies at the Boston City Hospital. Thus the average incidence was about 1 case in every 300 autopsies. Of these 25 cases, 7 were discarded because of inadequate clinical records.

HISTORICAL NOTES.

Whereas most of the vascular syndromes of the brain-stem have been the subject of a voluminous literature, basilar artery occlusion has

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received little attention. The first paper concerning this matter was that of Hayem (1868) who described the pathological anatomy of a single case but did not include an account of the clinical picture.

Leyden (1875) reported 2 autopsied cases of thrombosis of the basilar artery presumably due to a syphilitic endarteritis. Clinically there was an abrupt onset of hemiplegia followed by quadriplegia and bulbar palsies. In each case the eyes wandered separately, the pupils were unequal and would not react to light, the face and tongue were weak, speech was slurred and swallowing was impossible. Coma supervened, the temperature rose terminally to a high level, respirations became slow and irregular, and death occurred in about twenty-four hours in one case and after several days in the other.

Although sporadic case reports of basilar artery occlusion appeared in the literature during the next thirty-five years, the next important article was that by Marburg (1911) who presented an exposition, remarkably complete for its time, of this and other vascular syndromes of the brain-stem. He described the blood supply of the pons, the form and location of softenings produced by thrombosis of the basilar artery and its branches, outlined some of the clinical manifestations and appended a complete bibliography.

In recent years the outstanding contributions to our knowledge of brain-stem vascular syndromes were made by French workers. In 1926 Foix and Hillemand in connection with a study of pontine infarcts demonstrated the arterial supply of the pons and mid-brain by well-executed injections. On the basis of their observations they defined two syndromes, one of the paramedian territory which was manifested by a simple hemiplegia or, if bilateral, a quadriplegia, and the other, a lateral tegmental syndrome with crossed hemiplegia or crossed sensory and ipsilateral cerebellar signs. They also reported pathological cases in some of which the infarcts were probably due to occlusion of the basilar artery.

More recently, Lhermitte and Trelles (1933) published an account of arteriosclerosis of the basilar artery and its clinical consequences. They reported cases of so-called pontine hemiplegia due to unilateral paramedian softenings and of pontine quadriplegia due to similar bilateral involvement. When the softenings were more laterally placed and bilateral, a symptom complex with bilateral cerebellar and pyramidal tract signs occurred. This they designated as a pontocerebellar pseudobulbar palsy. In some of their cases the basilar artery or several of its main branches had undergone thrombosis. They agreed with Foix and Hillemand on the details of the blood supply to the pons and mid-brain.

The most completely examined case of basilar artery thrombosis is that of Pines and Gilinsky (1932). Serial sections of the brain-stem were made and the exact limits of the softenings were defined. In this case the upper third of the basilar artery was thrombosed and the softening involved the base of the pons bilaterally and the ventromedian part of the tegmentum. The clinical manifestations in this case had been abrupt onset of headache, dizziness and dysarthria, followed on the second day by coma, left hemiplegia and bilateral extensor plantar reflexes, and subsequently by high fever and death on the fourth day.

Other interesting case reports have appeared from time to time and have served only to verify previously reported observations. Seldom was the correct diagnosis made during life.

Report of Cases.

Case 1 (A10521—M.G.H.).—Male, aged 51.

History.—On the evening of August 21 the patient suddenly experienced numbness and tingling of fingers and toes and lips on the right side. He was overcome with fatigue and spent a restless night. The next morning his speech was thick, he had diplopia and was unsteady on his feet, almost falling while walking to the bathroom.

Examination.—At this time his physician noted that there was no impairment of consciousness. Both eyelids drooped; the pupils were of medium size, the right being larger than the left; nystagmus was present. Speech was indistinct; the plantar reflexes were bilaterally extensor. That same evening the patient was drowsy and had an almost complete paralysis of ocular movements on both sides. The pupils were now "pin-point." Both sides of the face were weak as were also the tongue, palate, jaw and neck muscles. The tendon reflexes were lively, more so on the right, and plantar reflexes were still extensor. Motor power in the limbs was reduced very little and co-ordination of movements was normal. All modes of sensation including hearing and vision were intact.

Laboratory data.—The cerebrospinal fluid pressure was normal; no cells were present and the total protein was 50 mg. per 100 c.c. The white blood cell count was 18,000 of which 87 per cent were polymorphonuclear leucocytes. The urine was normal and the Wassermann in blood and spinal fluid was negative.

Course.—On August 24, the condition of the patient was improved. He was more alert; both eyelids could be elevated but there was a paralysis of conjugate ocular movements upwards, downwards and to the left. The pupils were small and reacted normally. The movements of all four limbs were strong and the plantar reflexes were now equivocal. On August 27, improvement was still more marked and movements of the face, tongue and neck were stronger. That evening the patient again complained of paræsthesia of the right hand and face. The following morning he felt dizzy and more drowsy. The eyelids drooped to a greater degree, the pupils were contracted, and speech was almost inarticulate. Soon both sides of the face, both arms and both legs became paralysed. Urine was retained making catheterization necessary. The plantar reflex was flexor on the right and extensor on the left side. Shivering was noted and the breathing became rapid even though the temperature remained at 98·6°F. Within the next hour the patient became

comatose and remained so until his death the following day. Terminally the temperature was 100·8°F. The total duration of illness was eight days.

Anatomical diagnoses.—Thrombosis of the basilar artery; infarction of the pons and portions of the mid-brain (cf. fig. 1[1]); moderate atherosclerosis of the aorta, coronary arteries and cerebral arteries; pulmonary œdema and early bronchopneumonia.

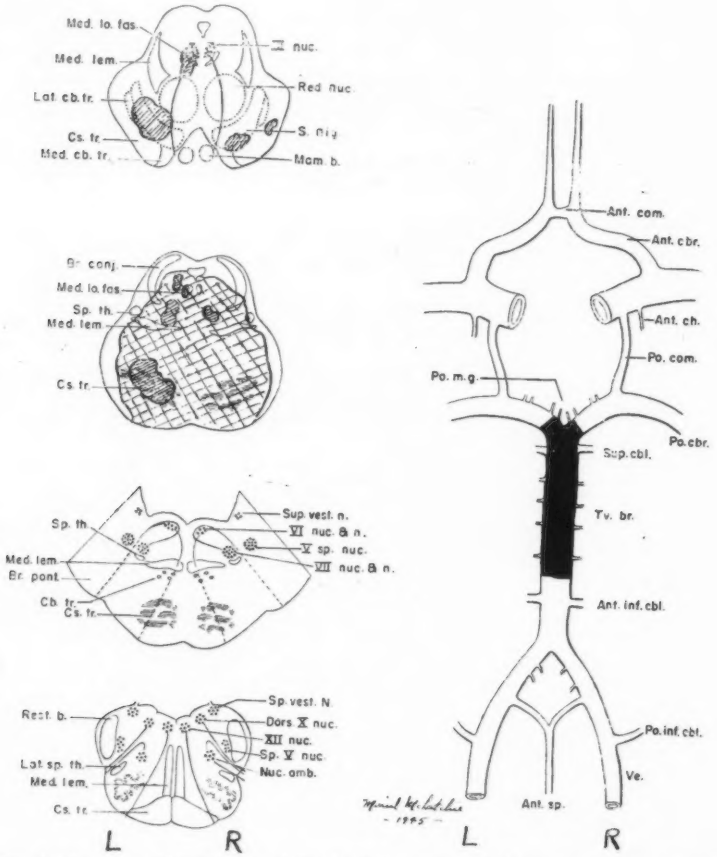

FIG. 1 (*Case* 1).—Thrombosis of the basilar artery. Sudden onset of paræsthesia, right side. 2nd day: Unsteady gait and diplopia. Later: Drowsiness, stupor, ptosis of eyelids, unequal pupils, paralysis of conjugate gaze, dysarthria, bilateral extensor plantar reflexes. 3rd-6th day: Improved. 7th day: Paræsthesia and dizziness, anarthria, quadriplegia coma. 8th day: Death.

[1]The shaded areas in the diagrams of the brain-stem indicate foci of complete necrosis. No attempt is made to represent nerve-cell changes and other signs of circulatory disturbance which were present in most of the cases.

Pathology.—The upper two-thirds of the basilar artery was occluded by a dark red thrombus which extended for a few mm. into both posterior cerebral arteries. The pons and mid-brain were soft, particularly on the left side, and on their cut surfaces a few petechial hæmorrhages and several small, fairly discrete foci of greyish discoloration were visible. These foci proved on microscopic examination to be infarcts and contained numerous microglial phagocytes (*see* fig. 2, Plate XI). In addition in almost the entire base and tegmentum of the pons there were shrunken eosinophilic nerve cells and pyknotic glia-cell nuclei, representing more recent infarction.

Comment.—Apparently the blood supply to the occipital lobes and optic thalami was maintained by collateral circulation through the posterior communicating arteries.

The oldest part of the lesion was in the left upper pons and mid-brain and so accounted for the earliest symptoms consisting of ocular palsies, dysarthria and paræsthesia of the right side of the body. Apparently the thrombus began in the upper third of the basilar artery and later propagated downwards, finally obstructing the blood supply to the greater part of the pons.

The lowest part of the pons and the medulla were normal and so the weakness of the lower face, the dysphagia and dysarthria were unquestionably due to bilateral involvement of the corticobulbar tracts (pseudobulbar paralysis).

Case 2 (A11352—M.G.H.).—Male, aged 58.

History.—Two weeks before admission to the out-patient clinic the patient, who had been well, served as a blood donor. During the withdrawal of blood and the rest of that day he felt all right but the following morning he became confused. Afterwards he had no memory for what had happened during the period of confusion. Two days later he had a dull steady pain in the crown of his head which later in the day settled in the frontal region. His vision became dim and blurred at this time. The headache disappeared in a few days but dimness of vision persisted. Two days before admission confusion increased and difficulty in swallowing and talking developed.

Examination.—B.P. 140/80. The patient appeared alert and answered questions appropriately. His speech was indistinct. The pupillary reactions and optic discs were normal. There was a left homonymous hemianopia and a partial lower right homonymous hemianopia. Ocular movements were normal. There was slight weakness of the right side of the face. Motor power, co-ordination of movements, reflexes and sensation were normal.

Course.—Patient was sent home from the out-patient clinic but was brought back the next day because he had become very drowsy and could not make himself understood. He had indicated that there was no "feeling" in his right arm and around his mouth. On examination he was stuporous and his speech was mumbling and incoherent; respirations were slow and irregular; pupils were small and reacted hardly at all to light. No record of ocular movements was made. There was marked weakness of the face and paralysis of the arm and leg on the right side and only a few feeble movements of the arm and leg on the left side. A satisfactory sensory examination was not possible because of the patient's mental condition.

Tendon reflexes were absent on the right and present on the left side; abdominal reflexes were absent and plantar reflexes were extensor bilaterally. The cerebrospinal fluid was under normal pressure; there were no cells; total protein was 55 mg. per 100 c.c.; and gold sol and Wassermann reactions were negative. The white blood count was 16,000 per c.mm. The day after admission or on seventeenth day of the illness, the patient became comatose and died.

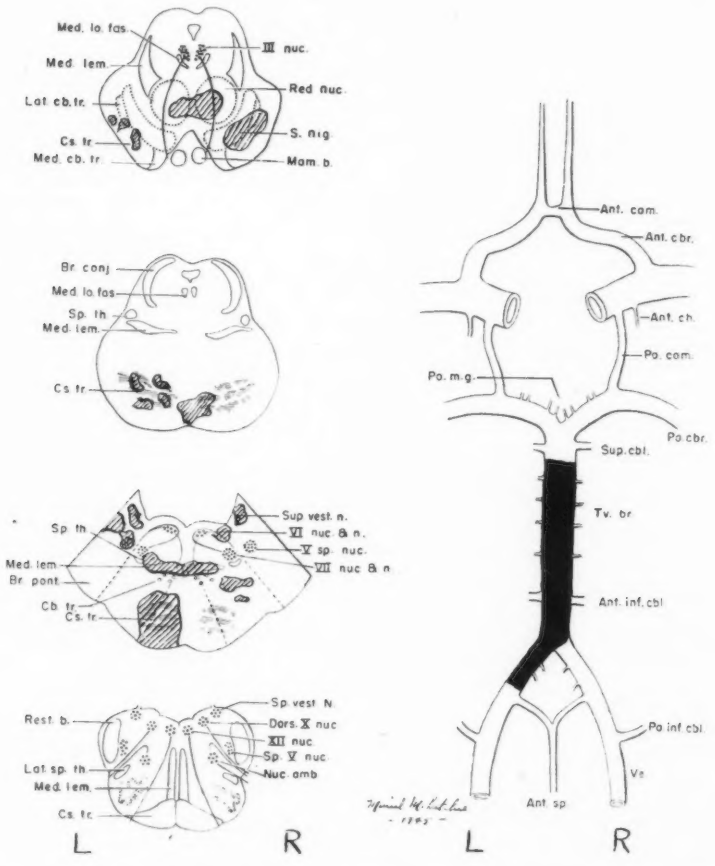

FIG. 3 (*Case* 2).—Thrombosis of the basilar and left vertebral artery. Blood donation. 2nd day: Confusion for a few minutes. 4th day: Headache and dimness of vision. 12th day: Increased confusion and forgetfulness, dysphagia and dysarthria. 15th day: Drowsy, severe dysarthria, left and partial right homonymous hemianopia, right hemanæsthesia, right hemiplegia and left hemiparesis, bilateral extensor plantar reflexes. 17th day: Coma and death.

Anatomical diagnoses.—Generalized atherosclerosis; thrombosis of basilar artery; infarction of pons, mid-brain and occipital lobes.

Pathology.—A thrombus filled the upper 1 cm. of the right vertebral artery and the greater portion of the basilar artery, extending not quite to the superior cerebellar arteries. There were destruction of myelin and necrosis of nerve cells and glia cells of the pons and mid-brain (cf. fig. 3). These lesions were quite recent; there were as yet no microglial phagocytes. In the right calcarine cortex there was a considerably older infarct, estimated to be two or three weeks old as judged by the presence of numerous microglial phagocytes.

Comment.—Some features of this case, such as the early mental confusion and impairment of memory, are not easy to understand. The blurring of vision and visual field defects are explained by infarction of the calcarine cortex, though it is not clear why the only lesion of that age was in the right occipital lobe. One possibility would be that a small embolus became detached from a thrombus which had begun to form in the basilar artery; another would be inadequate collateral circulation. The quadriplegia is easily correlated with the recent infarction of the pons and mid-brain. It is of some interest that onset of symptoms followed shortly after a blood donation.

Case 3 (A43-162—B.C.H.).—Male, aged 39.

History.—Shortly before entry, while eating at a restaurant, the patient complained of momentary dizziness. About half an hour later he again felt dizzy, and suddenly "collapsed." He was taken home where it was observed that the left arm and leg were paralysed, and was then brought to the hospital. There was an occasional twitching of the right arm and leg. He vomited several times.

In the preceding few months the patient had had several dizzy spells, each lasting a few seconds. Following one of these he had a convulsive seizure following which there was weakness of the left arm and leg for a few hours.

Examination.—T. 98°F., P. 108, R. 24, and B.P. 120/80. When admitted the patient was unable to speak. He was stuporous. There was a constant spontaneous horizontal nystagmus. The eyes rolled from side to side and sometimes moved independently of each other. At times skew deviation was thought to be present. There was some lateral deviation of the left eye. The optic discs and retinal vessels appeared to be normal. The pupils were small, unequal and did not react to light. Corneal reflexes were present. In breathing, air was expired mostly through the left side of the mouth. The tongue deviated slightly to the right. There was marked weakness but not a complete paralysis of the left arm and leg. The right arm and leg were moved well. Tendon reflexes were equal and active, and plantar reflexes were extensor bilaterally. The neck was not stiff.

Laboratory data.—The urine was normal. The hæmoglobin on entry was 113 per cent., and white count 20,000. The differential count was 81 per cent. polymorphonuclear leucocytes, 14 per cent. lymphocytes, 5 per cent. monocytes. The non-protein nitrogen was 27; the fasting blood sugar, 110. Blood Hinton test was negative. The cerebrospinal fluid on entry was under a pressure of 129; it contained 2 lymphocytes and a total protein of 22 mg. per 100 c.c.

Soon after entry, the patient became more alert and was able to talk, but had marked dysarthria. Twelve hours after entry he was again stuporous. The bizarre, inco-ordinated eye movements continued. Twenty-four hours after entry, he had

Cheyne-Stokes' respirations and was cyanotic. At this time there were several episodes in which all four extremities were rigidly extended for several minutes, and which were thought by the attending physician to represent decerebrate rigidity. The blood-pressure varied from 110/70 to 180/100. Stupor progressed to coma and on the seventh day of his illness cyanosis increased markedly, respirations became very rapid and shallow, the temperature rose to 106°F. and the patient died.

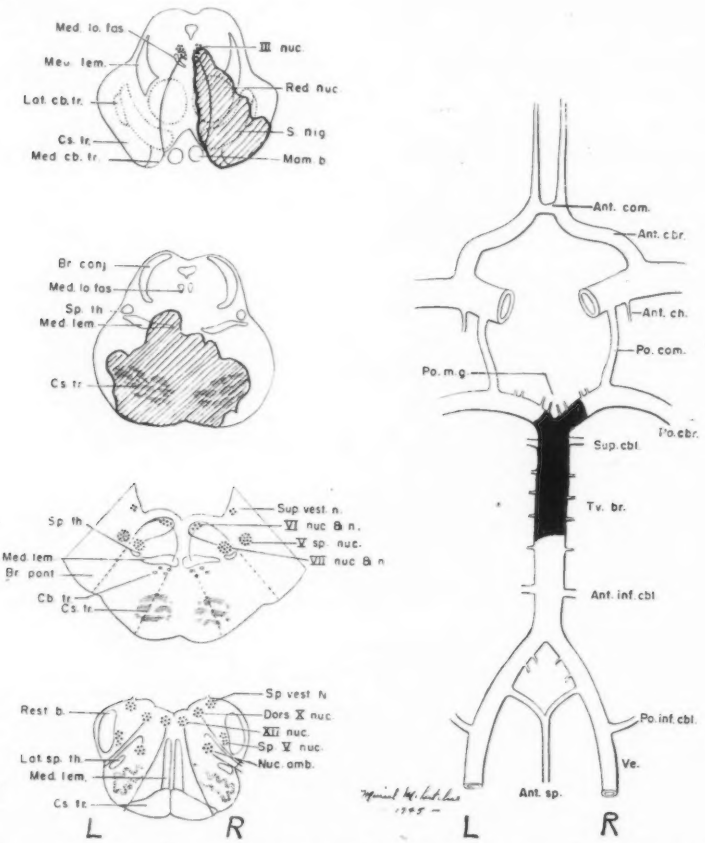

FIG. 4 (*Case* 3).—Thrombosis of basilary artery. Sudden onset of dizziness, nausea and vomiting. 3 hours later: deep stupor, anarthria, divergent strabismus, left hemiplegia, bilateral extensor plantar reflexes. 36-48 hours later: Quadriplegia, tonic convulsions with extension of all four limbs; deep coma, T. 106, R. 50. 7th day: Death.

Anatomical diagnoses.—Generalized atherosclerosis; thrombosis of the basilar artery; infarction of pons, mid-brain and cerebellum (cf. fig. 4).

Pathology.—The upper half of the basilar and the first few mm. of both posterior cerebral arteries were filled with a red thrombus. The posterior communicating arteries were of good size and patent. The base of the pons bilaterally, the right half of the mid-brain and superior portions of both cerebellar hemispheres were soft (cf. fig. 5 upper left, Plate XI). In these parts nerve and glia cells were destroyed and many microglial phagocytes were present. There was early fibroblastic invasion of the thrombus.

Comment.—The clinical signs were accounted for by infarction of structures in the pons and mid-brain. No lesion was found to explain the convulsive seizure and transient left hemiparesis which occurred several months before death.

Case 4 (NP44-35—B.C.H.).—Male, aged 51.

History.—For several years the patient had been having attacks of vertigo, presumably of labyrinthine origin. He entered the hospital this time because of nervousness and easy fatigability. On the evening of the fourth hospital day he became apprehensive and complained of a dull occipital headache and paræsthesia of the left side of the body. During the night he was restless and about 6 a.m. was found by the nurse, sitting on the floor, confused and unable to speak distinctly.

Examination (Twenty-four hours after onset).—T. 99·2°F.; P. 80; R. 22; B.P. 116/80. Although able to converse with the examiner, the patient was confused and his speech was poorly articulated. The pupils were small, equal in size, and reacted to light and convergence. Ocular movements were normal. Movements of the right hand were slightly weak and there was ataxia of left arm and leg. Motor power in both arms and legs was normal. The tendon reflexes which had been difficult to obtain at the time of entry were now lively, more so on the left than on the right side, and the abdominal reflexes, which had been present, were now absent. Plantar reflexes were flexor. Sensation of light touch was impaired in the left foot but vibration and position senses were retained on both sides.

Laboratory data.—Cerebrospinal fluid: initial pressure was 250 mm.; no cells were present; total protein was 57 mg. per 100 c.c.; Wassermann and colloidal gold tests were negative.

Course.—The following day the patient lapsed into deep coma. His eyes were turned to the left. The pupils were equal in size and reacted to light. Muscle tone was diminished in the right arm and leg. The tendon reflexes were approximately equal but the plantar reflex was equivocal on the right side and flexor on the left side. Breathing was deep and stertorous. Death occurred on the third day of the illness.

Anatomical diagnoses.—Generalized atherosclerosis; thrombosis of basilar artery; infarction of pons and cerebellum (cf. fig. 6); healed coronary thrombosis and old apical cardiac infarct.

Pathology.—The lower half of the basilar artery was occluded by a dark red thrombus which in microscopic section was just beginning to undergo fibroblastic organization. The pons was soft at the level of the trigeminal nerves. The mid-brain, optic thalami and occipital lobes were normal, probably because of collateral circulation through the posterior communicating arteries, which were of normal size.

Comment.—The absence of any disorder of ocular movements or pupils, the difficulty in demonstrating paralysis of the limbs and the relatively slight alteration of reflexes made clinical diagnosis difficult. However

there were abnormal signs on both sides of the body, i.e. left-sided paræsthesias, and the questionable right hemiparesis which should have suggested that the brain-stem was the site of the lesion. The initial dysarthria and paræsthesias of the left side of the body were probably caused respectively by involvement of the corticobulbar tracts bilaterally

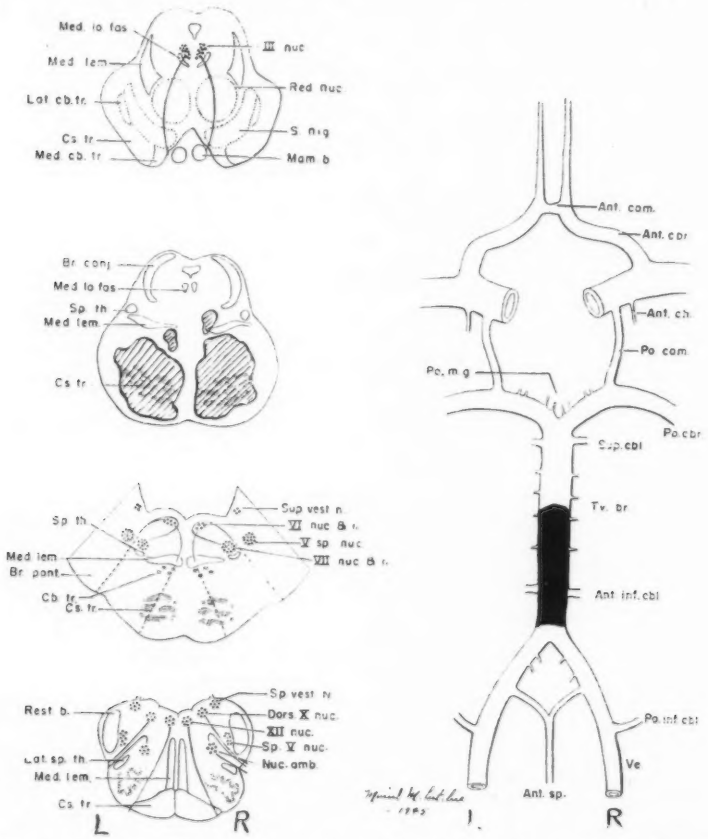

FIG. 6 (*Case* 4).—Thrombosis of the basilar artery. Acute onset of occipital headache, paræsthesias of left side of body. 6 hours later: Confusion, dysarthria. 24 hours later: Greater confusion, weakness of right arm, ataxia of left arm and leg, hypæsthesia, left foot. 2nd day: Deep coma, stertorous respirations, head and eyes turned to the left, right hemiplegia, extensor plantar reflex on right. 3rd day: Death.

and the right medial lemniscus. The signs which developed later were presumably due to more extensive involvement of the pons and mid-brain.

There is a clear indication that the headache was related to the thrombosis since it was coincident with the onset of other symptoms and the history stated that the patient had never before had a headache.

Case 5 (A42-448—B.C.H.).—Female, aged 64.

History.—At 10 p.m.—two days before admission to the hospital this patient suddenly became weak and dizzy. During the night she was nauseated, vomited

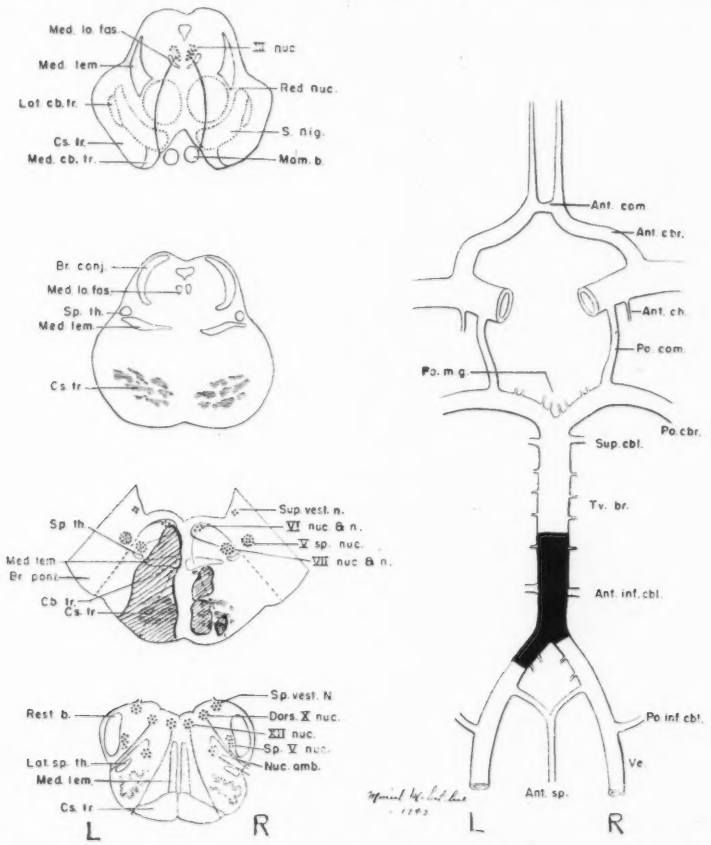

FIG. 7 (*Case 5*).—Thrombosis of the basilar artery. Sudden onset of weakness, dizziness, vomiting; frontal headache. 3rd day: Drowsiness and confusion, dysarthria, left abducens paralysis, left facial paralysis and right hemiplegia. 13th day: Sudden circulatory collapse, coma and death (pulmonary embolus).

several times and developed a dull headache. The next morning her speech was slow and indistinct. For the preceding four years the patient had had "dizzy" spells which were attributed to arterial hypertension.

Examination.—T. 98°F.; P. 65; R. 22; B.P. 210/110. The patient was conscious and there was no confusion or impairment of memory. There was a severe dysarthria. The pupillary reflexes and ocular movements were normal. There was central streaking, a-v nicking and tortuosity of the retinal arteries. The left side of face was weak and there was a right hemiparesis with diminished tendon reflexes and an extensor plantar reflex. The heart was enlarged and the second aortic sound was accentuated.

Laboratory data.—Urine: Specific gravity was 1,020; tests for albumen and sugar were negative. White blood count was 10,800 with 78 per cent. polymorphonuclear leucocytes. Cerebrospinal fluid was under normal pressure; protein was normal and the Davies-Hinton and Wassermann tests were negative. The electrocardiogram showed evidence of myocardial disease.

Course.—On the third day in the hospital left abducens and facial nerve palsies and right hemiparesis had developed. The patient was irrational. She struggled to get out of bed and once fell out. Several times she took off her clothes and sat naked in the open ward.

On the eighth hospital day (tenth day of illness) she suddenly lost consciousness while being placed in a chair. She was pale and slightly cyanotic. The pupils were small and fixed to light. Corneal reflexes were absent. The limbs were flaccid. In a few minutes she regained consciousness and had active pupillary and corneal reflexes. Two days later she complained of pleuritic pain, and a friction rub was heard in the right side of the chest. On the eleventh hospital day (thirteenth day of illness) coma recurred, respirations became feeble and gasping, and the patient died.

Anatomical diagnoses.—Generalized atherosclerosis; thrombosis of the basilar artery; infarction of pons; hypertensive and arteriosclerotic heart disease; thrombosis of popliteal veins of right leg; bilateral multiple pulmonary emboli with pulmonary infarction.

Pathology.—The upper part of the left vertebral artery and the inferior half of the basilar artery were filled with a red thrombus. The lower portion of the pons, especially the left half of it, was very soft (cf. fig. 7). The mid-brain, cerebellum, optic thalami and occipital lobes were not affected.

Comment.—Microscopic examination indicated that the earliest lesion was in the left half of the pons and so corresponded to the left facial and abducens paralysis and the crossed right hemiplegia. Eventually there was more extensive infarction involving both sides of the pons. Possibly the thrombus began on one side of the basilar artery, occluding only one or two small pontine branches, and later extended until it completely filled the entire lumen. The two episodes of circulatory collapse and coma, the last one of which was fatal, were probably caused by pulmonary embolism.

Case 6 (A44-037—B.C.H.).—Female, aged 48.

History.—Ten days before entry this patient, a coloured woman with diabetes, began to have vertigo, tinnitus in both ears, a severe occipital headache and frequent crying spells. Three days before entry the headache and vertigo grew more severe and her legs became so weak that she could walk only with assistance. On the day of hospital admission she awakened to find her right arm and leg completely paralysed.

Examination.—T. 98·6°F.; P. 80; R. 60; B.P. 210/110. The patient was conscious and rational. She talked spontaneously and answered questions adequately but her speech was badly slurred. The pupils were equal in size and reacted to light and on convergence. No disturbance of ocular movements was noted. The retinal

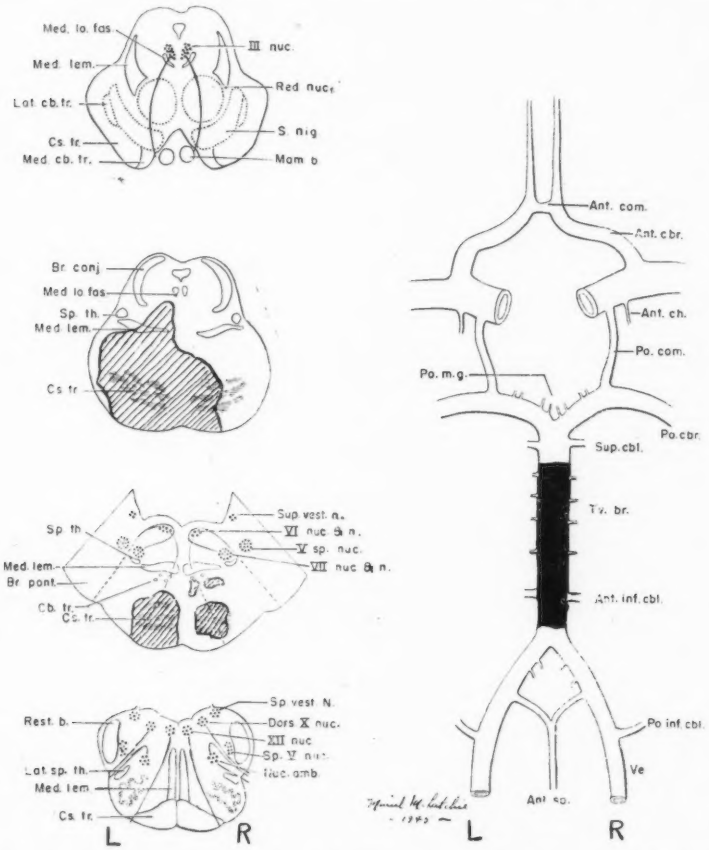

FIG. 8 (*Case* 6).—Thrombosis of basilar artery. Sudden onset of vertigo, tinnitus in both ears, occipital headache. 3rd day: Weakness of legs; crying spells. 10th day: Right hemiplegia, dysarthria and dysphagia, impaired vibratory and position senses—right arm and leg. 11th to 17th day: Improvement. 18th day: Coma, pupils fixed, left one dilated, bilateral extensor plantar reflexes. 19th day: Death.

arteries were sclerotic and there was one small hæmorrhage in the right eye. The visual fields were not examined. There was a paralysis of the right side of the face including frontalis and orbicularis oculi muscles. The tongue protruded to the

right. There was a flaccid paralysis and impairment of touch, vibration and position senses in right arm and leg. Pain and temperature sensation were preserved. The tendon reflexes were reduced on the right; the plantar response was extensor on the right and equivocal on the left. The patient was incontinent of urine.

Laboratory data.—Cerebrospinal fluid was under normal pressure, contained 7 cells per c.mm. and was otherwise normal. The urine gave a 3+ positive test for sugar.

Course in hospital.—During the first five or six days there was some return of strength in the right arm and leg. Difficulty in swallowing necessitated the use of a stomach tube several times. On the eighth day in hospital (eighteenth day of illness) the patient became unconscious. The left pupil was dilated and both pupils were fixed to light. Breathing was rapid. Plantar reflexes were extensor on both sides. Death occurred on the ninth hospital day, nineteen days after onset of vertigo, tinnitus and headache and twelve days after onset of weakness of the legs. The temperature was never above 99°.

Anatomical diagnoses.—Cerebral and coronary atherosclerosis; thrombosis of basilar artery; infarction of pons; diabetes mellitus; arteriosclerotic heart disease with myocardial fibrosis.

Pathology.—There was such a marked degree of atherosclerosis that the lumen of the lowest part of the basilar artery was almost completely obliterated. This part and the remaining lower two-thirds of the basilar artery was filled with a firm, dark red thrombus. The left side of the pons was soft and its cut surface was greyish in colour and stippled with a few petechial hæmorrhages (cf. fig. 8). There were several small, old infarcts from 0·5 cm. to 1·0 cm. in diameter in the right cerebellar hemisphere and in both lenticular nuclei. The occipital lobes and optic thalami were normal.

Comment.—Perhaps one cannot be certain that the tinnitus and vertigo were related to the thrombosis of the basilar artery, but occurring as they did in association with the headache and increasing in severity with the onset of more typical symptoms it seems likely that they were. A beginning thrombosis in the lower part of the basilar artery might have interfered with the blood flow in branches to the inner ears. The softening was more extensive on the left side of the pons thus corresponding to the right hemiplegia and sensory impairment. Although there was no definite lesion in the mid-brain, the pupillary disturbances which coincided in time with the loss of consciousness were presumably due to a circulatory insufficiency causing derangement of function but not severe enough to produce demonstrable pathological changes.

Case 7 (A6656—M.G.H.).—Male, aged 60.

History.—Early in the morning of the day of admission this patient, who had previously had occasional dizzy spells, suddenly lost consciousness and fell to the floor. The length of time he was unconscious was not recorded, but he had regained consciousness before entering the hospital.

Examination.—On entry T. 99°F.; P. 86; R. 20; B.P. 180/110. The patient was conscious and capable of understanding what was said, but his speech was inarticulate. The pupils were constricted and did not react to light. The retinal arteries were tortuous and sclerotic. The face was thought to be paralysed bilaterally and

the strength of both arms was exceedingly feeble. The tendon reflexes were very brisk and the plantar reflexes were extensor bilaterally.

Course.—On the following morning the patient lapsed into deep coma. Temperature rose to 108·2°F. and pulse to 140; respiration remained at 20. Blood-pressure fell to 60/40. Death occurred shortly afterwards, approximately thirty-two hours after the initial loss of consciousness.

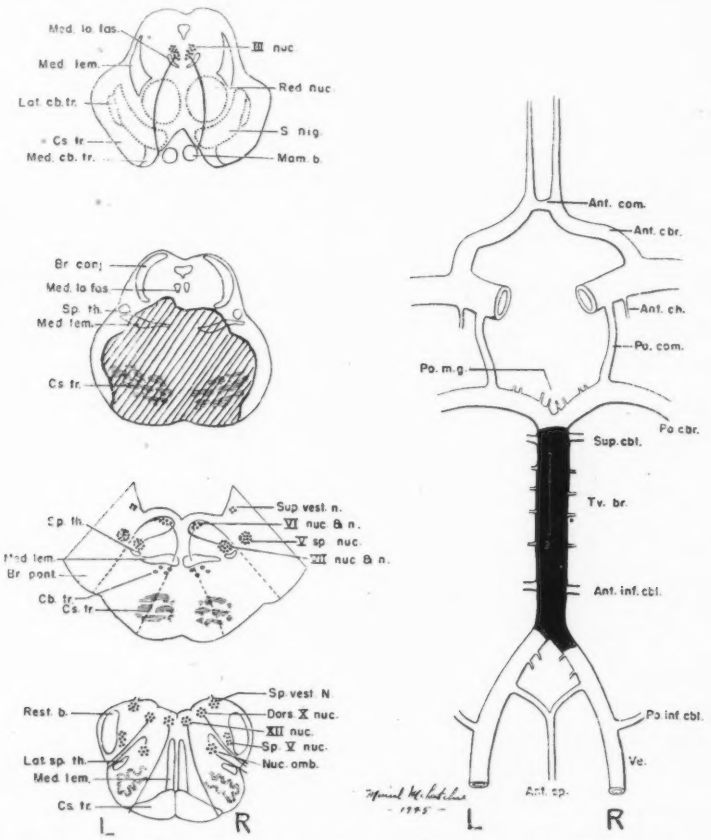

FIG. 9 (*Case* 7).—Thrombosis of basilar artery, sudden onset of coma. A few hours later: Return of consciousness, dysarthria, constricted pupils, bilateral facial weakness, quadriplegia, bilateral extensor plantar reflexes. 24 hours later: T. 108, P. 140, R. 20, B.P. 60/40. 32 hours later: Death.

Anatomical diagnoses.—Marked aortic and cerebral arteriosclerosis; thrombosis of basilar and right vertebral arteries; infarction of pons (cf. fig. 9); multiple small organized infarcts of basal ganglia and cerebellum; pulmonary œdema and congestion; cardiac hypertrophy and dilatation, left ventricle, hypertensive type.

Pathology.—There was an extreme degree of atherosclerosis of the basilar and internal carotid arteries; the walls were thickened and the lumens were narrowed almost to the point of occlusion in many places. Throughout the length of the basilar artery there was a dark red thrombus which extended for a short distance into the right vertebral artery. The base of the pons was slightly soft. In microscopic section there were the usual findings of recent infarction. The lower pons, medulla, mid-brain, optic thalami and occipital lobes were normal.

Comment.—The bilateral corticospinal tract and bilateral corticobulbar tract signs which characterized the patient's illness are adequately explained by infarction of the upper half of the pons. The infarction was so recent that its full extent probably could not be determined. The small fixed pupils are of interest in the absence of demonstrable pathology in the mid-brain: they may be explained by a circulatory disorder not severe enough to produce histological changes. Another explanation of the small pupils might be an interruption of the descending pupillodilator fibres at the level of the pons. The minute, old infarcts in the cerebellar cortex and lenticular nuclei undoubtedly played no part in the symptoms of the terminal illness.

Case 8 (A9420—M.G.H.).—Female, aged 73.

History.—For several years this elderly woman had been treated in the outpatient department of the Massachusetts General Hospital for coronary heart disease with angina pectoris and for diabetes mellitus. On December 6 she entered the hospital complaining of sudden failure of vision and frontal headache of five days' duration.

Examination.—T. 100°F.; P. 70; R. 20; B.P. 174/90. The patient was oriented and rational but her mood was labile. There was aphakia bilaterally. The retinal arteries were arteriosclerotic, and the nature of the impairment of vision was not determined. The only abnormal neurologic findings were absent knee and ankle jerks and impairment of vibratory and position senses over the feet.

Laboratory data.—White blood cell count was 18,000 of which 80 per cent. were polymorphonuclear leucocytes. Urine gave a positive 1 to 2+ test for sugar. Fasting blood sugar was 140 to 268 mg. per 100 c.c. Electrocardiogram was normal. Cerebrospinal fluid: pressure was 110 mm.; there were no cells; total protein was 48 mg. per 100 c.c.; Wassermann reaction was negative.

Course.—On the fifteenth hospital day the nurses noticed that the patient was "acting queerly and not responding well." She was found to have a left flaccid hemiplegia affecting face, arm and leg. There was subsequently temporary improvement in her mental status, but within a few hours she lapsed into coma. Following that the right eye was partially closed while the left was open, and there was now a flaccid paralysis of all four extremities with extensor plantar reflexes bilaterally. Temperature rose to 102° and pulse to 150. Respirations were 30. Death occurred two days later or fifty-three hours after the onset of paralysis and twenty-three days after onset of headache and impairment of vision.

Anatomical diagnoses.—Marked cerebral and moderate coronary and aortic arteriosclerosis; thrombosis of the vertebral and basilar arteries; infarction of the medulla, pons and mid brain, left cerebellar hemisphere, and left occipital lobe; diabetes mellitus (clinical).

Pathology.—The basilar artery was filled with a firm pale reddish thrombus which blocked off the superior and middle cerebellar arteries and extended into both vertebral arteries, below the left, but falling short of the right posterior inferior cerebellar artery. The right posterior communicating artery was very small: the left was normal. There was softening of the entire left cerebellar hemis-

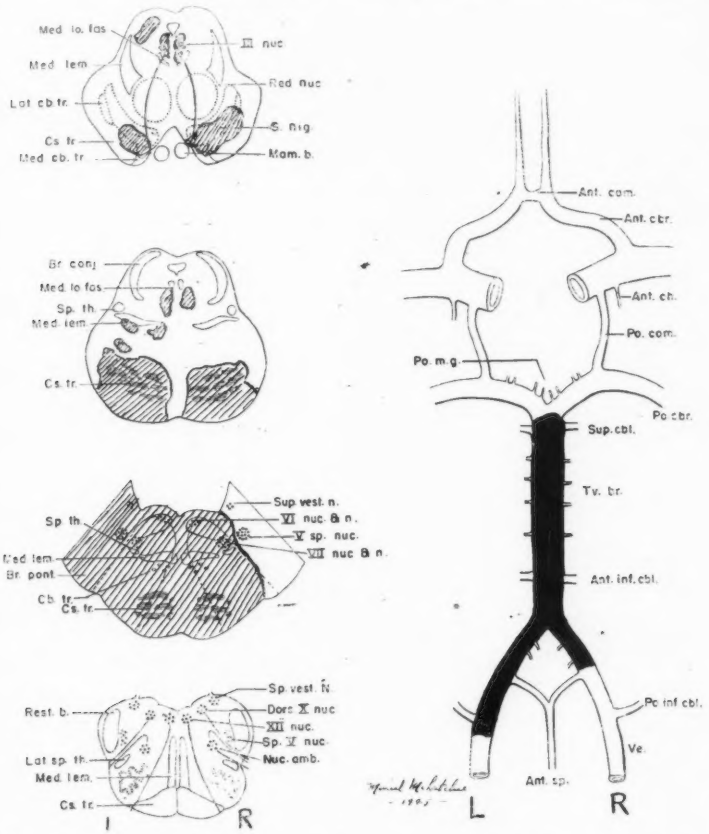

FIG. 10 (*Case* 8).—Thrombosis of the vertebral and basilar arteries. Sudden onset of impaired vision, frontal headache. 5th to 19th day: Improvement. 20th day: Confusion, right oculomotor palsy, left hemiplegia. 21st day: Coma, quadriplegia, bilateral extensor plantar reflexes. 23rd day: Death.

phere, the left restiform body and both sides of the base of pons and of lower portion of the mid-brain (cf. fig. 10). The optic thalami were normal. One focus of hæmorrhagic discoloration measuring 1·0 to 1·5 cm. in diameter was found in the left calcarine cortex. Microscopic examination of the thrombus in the left vertebral artery revealed that it was old and well organized; the thrombus in the

right vertebral artery was more recent and partly organized; and the thrombus in the basilar artery and first portion of the left posterior cerebral artery was recent and unorganized. All the foci of infarction, except the one in the occipital lobe which contained many microglial phagocytes, were recent.

Comment.—Impairment of vision, which in this case was the first symptom, probably represented cortical blindness. Unfortunately the visual fields were not examined but some confirmation of such a possibility was provided by the infarct in the left calcarine cortex. The ptosis of the right lid and the left hemiplegia correspond to the lesion in the right cerebral peduncle and the remainder of the symptoms were related to the pontine infarct. There was nothing in the past history corresponding to an old thrombosis of the vertebral artery. The impairment of vibratory and position senses in the feet and the absent knee and ankle jerks were presumably due to diabetic neuritis.

Case 9 (A44-184—B.C.H.).—Male, aged 53.

History.—Three days before entry to the hospital the patient became dizzy. Several hours later he noticed that his left arm and leg were paralysed and numb. There was no loss of consciousness. He had had recurrent headaches and dizzy spells for one year.

Examination.—T. 98°F.; P. 80; R. 25; B.P. 130/90. The patient was conscious and rational. His speech was slurred and indistinct. There were paralysis of external rotation of the right eye and crossed paralysis of the left arm and leg. The tendon reflexes were less active on the left side than on the right; abdominal reflexes were absent; and the plantar reflexes were extensor bilaterally. Vibratory and position senses were absent in the left arm and leg. The skin over the left side of the body was cool and moist and over right side it was warm and dry.

Laboratory data.—White blood cell count was 10,400. Hinton and Wassermann tests were positive. C.S.F.: pressure was 150 mm.; there were 12 lymphocytes per c.mm.; total protein was 81 mg. per 100 c.c.; Wassermann reaction was positive in 0·05 c.c. of fluid and Davies-Hinton was positive.

Course.—Shortly after admission the patient lapsed into coma. He became cyanotic and his temperature rose to 105°F. There were no movements of the arms or legs. Death occurred on the second hospital day or fifth day of his illness.

Anatomical diagnoses.—Generalized atherosclerosis; meningo-vascular syphilis; thrombosis of the basilar artery, infarction of the pons and cerebellum.

Pathology.—There was marked atherosclerosis of the large cerebral and basilar arteries. The lower two-thirds of the basilar artery was filled with a dark red thrombus. In addition to the pontine infarcts (cf. fig. 11) one small focus of softening, measuring 2 cm. in diameter was found in the left cerebellar hemisphere. The upper pons, mid-brain, optic thalami, occipital lobes and medulla were normal. Microscopic sections of the thrombosed artery revealed, in addition to advanced atherosclerosis, adventitial infiltration with lymphocytes and plasma cells. The leptomeninges contained similar cellular infiltrations and there was a granular ependymitis. The pontine and cerebellar infarcts of the same age were estimated to be two or three days old.

Comment.—Although there was a syphilitic meningitis and a slight inflammatory reaction in the adventitia of the basilar artery, it seemed

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that the atheromatous changes alone were adequate to account for the thrombosis. The lesion was more pronounced on the right side of the pons and it may be supposed that it began on this side, thus accounting

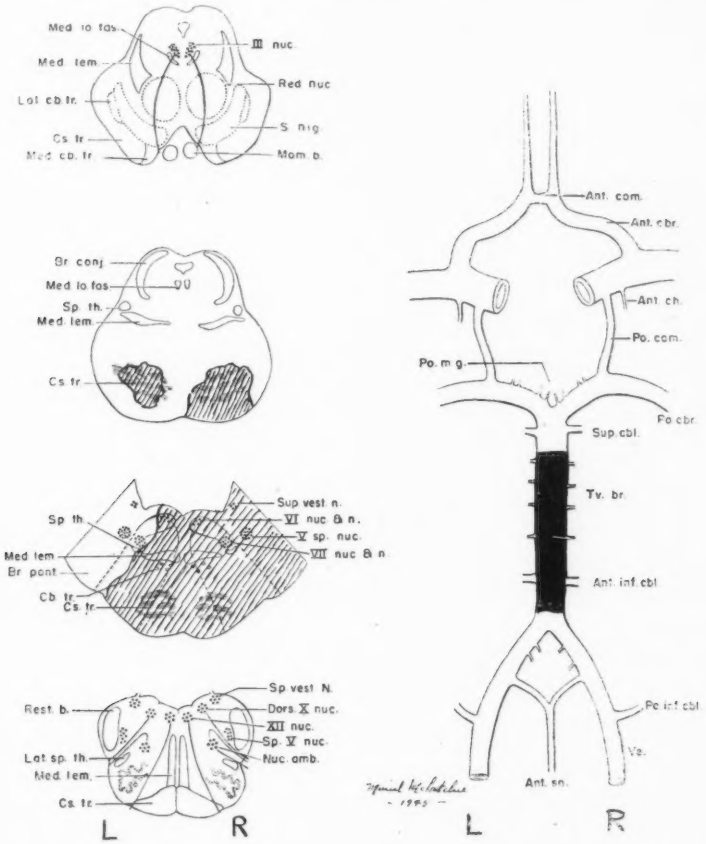

FIG. 11 (*Case* 9).—Thrombosis of the basilar artery. Sudden onset of dizziness. A few hours later: Dysarthria, right abducens palsy, numbness of left side of body, left hemiplegia, Bilateral extensor plantar reflexes. 2nd day: Coma, no movement of arms or legs; death.

for the unilateral abducens paralysis and crossed hemiplegia observed in the early part of the illness, while the onset of coma and bilateral cortico-spinal tract involvement indicated extension of the thrombosis and increase in the size of the infarct.

Case 10 (A44-532—B.C.H.).—Male, aged 77.

History.—About six weeks before entry the patient awakened with a scream in the middle of the night, urinated in bed, was unable to speak clearly, and the following day was observed to have weakness of the right side of his face. He rapidly improved and then, five weeks later, was found in a helpless state, unable

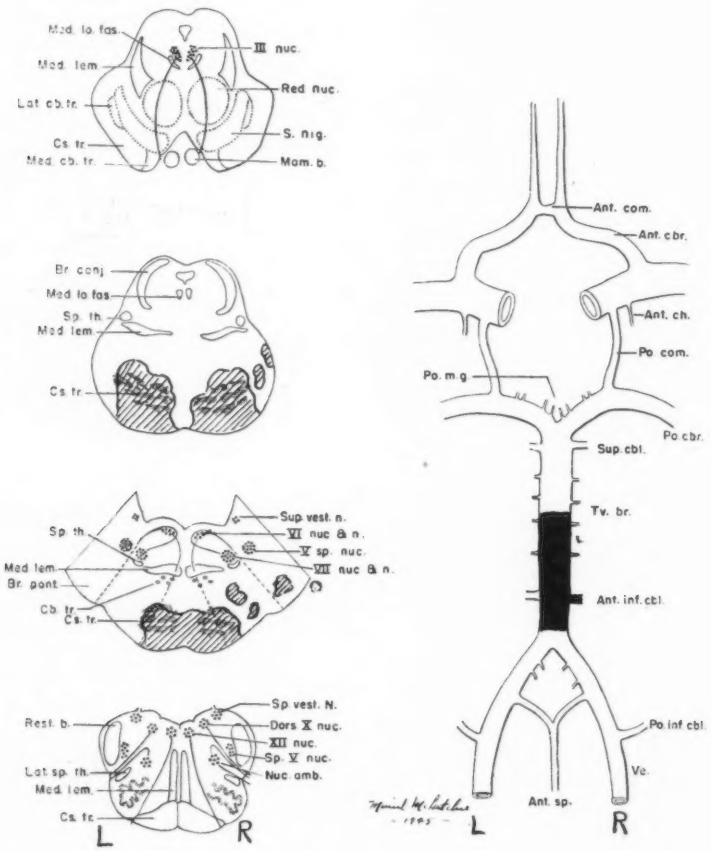

FIG. 12 (*Case* 10).—Thrombosis of the basilar and right middle cerebellar arteries. Sudden onset of dysarthria, urinary inconsistence, right facial weakness. Next 5 weeks: Improvement. Sudden relapse with confusion, dysarthria and dysphagia, right hemiplegia, bilateral extensor plantar reflexes. 12 days later: Death.

to walk or to speak clearly. He vomited several times and was confused and emotionally unstable. There had been little change in his condition at the time of admission one week later.

Examination.—T. 99·6°F.; P. 90; R. 20; B.P. 210/110. The patient's speech was unintelligible. He was able to perform simple tests on command. The pupils were equal in size and reacted to light. The retinal arteries were tortuous and irregular in outline with prominent light streaks. There were right facial weakness and weakness and spasticity of the right arm and leg. The tendon reflexes were more active on the right side; there was ankle clonus on the right, not on the left; and the plantar reflexes were extensor bilaterally. The heart was slightly enlarged to the left.

Laboratory data.— White blood count was 10,400. Cerebrospinal fluid: pressure was 200 mm.; there were no cells; protein was 18 mg. per 100 c.c.; Wassermann test was negative.

Course.—On the second hospital day the patient was feeble but conscious. His face was weak on both sides and saliva drooled from his mouth, but he was able to smile. Pharyngeal reflexes were absent and accumulated saliva and bronchial secretions failed to provoke coughing. On the fourth hospital day the patient became comatose, temperature rose to 104°F., respirations were rapid and laboured and death occurred several hours later, on the twelfth day of the illness.

Anatomical diagnoses.—Thrombosis of basilar and right middle cerebellar arteries; infarction of the pons and right cerebellar hemisphere; generalized atherosclerosis; bronchopneumonia.

Pathology.—The lower half of the basilar and the right middle cerebellar arteries were occluded by a brick red thrombus. The inferior portion of the right cerebellar hemisphere, the right middle cerebellar peduncle and base of the pons were of mushy consistence (cf. fig. 12). In large parts of the infarcted tissue nerve and glia cells had completely disappeared, and there was proliferation of capillary endothelial cells and microglial cells.

Comment.—There was an anomalous arrangement of the arteries; on both sides the posterior inferior and middle cerebellar arteries arose from a common trunk which had its origin from the lower basilar artery. Thus the extensive infarction of the right cerebellar hemisphere was explained, but the reason for lack of infarction of the left cerebellar hemisphere was not discovered. In injecting arteries of the brain we have sometimes found arterial anastomoses between the cerebellar arteries and believe that such a vessel would provide an explanation of the findings.

Case 11 (A45-271—B.C.H.).—Female, aged 68.

History.—For several years the patient had had headaches and dizziness. Five years before entry she was found to have diabetes mellitus which was controlled by diet. In the past year or two increasing nervousness, forgetfulness and lack of initiative had been noted by the patient's family. On the day before entering the hospital she had a "weak spell" after which she felt dizzy, had blurred vision and was unable to speak clearly.

Examination.—T. 99·4°F.; P. 68; R. 16; B.P. 184/84. The patient was confused and unable to give a history of her illness. Her speech was slurred. There was weakness of the entire left side of the face. Optic fundi, pupils and ocular movements were normal. Arms and legs were strong. Plantar reflex was normal on the right and doubtful on the left side. The heart was enlarged to the left and there were systolic murmurs over the aortic area and at apex.

Laboratory data.—White blood count was 5,500, rising to 14,500 on the fifth

hospital day. Cerebrospinal fluid: pressure was 160 mm.; there were no cells; total protein was 29 mg. per 100 c.c., Wassermann and Davies-Hinton tests were negative.

Course.—On the third hospital day (fourth day of illness) the patient became stuporous. Her right arm and leg were paralysed and flaccid. The plantar reflex

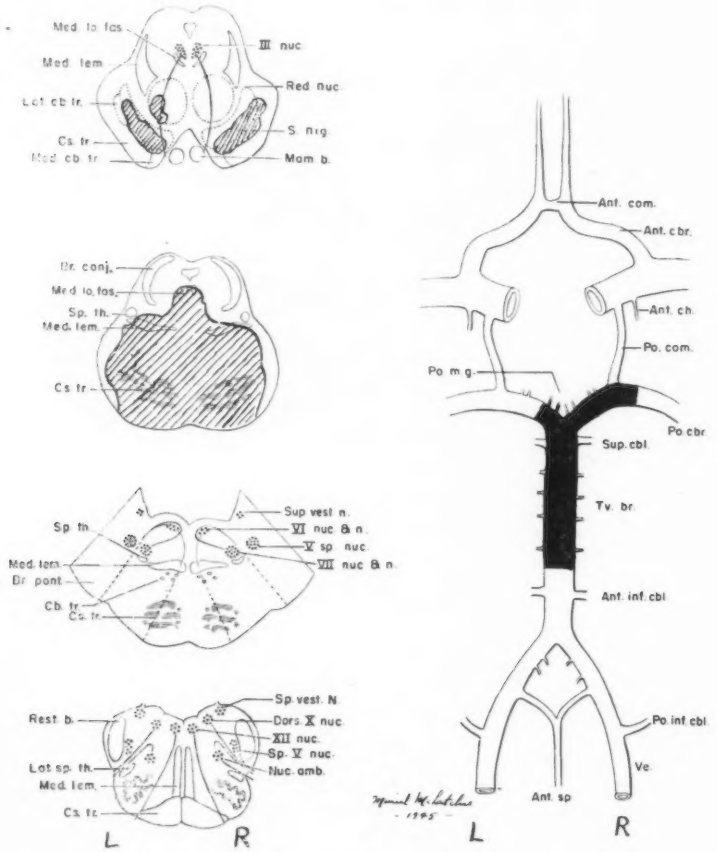

FIG. 13 (*Case* 11).—Thrombosis of the basilar and right posterior cerebral arteries. Sudden onset of dizziness, blurred vision, dysarthria, weakness of the left face. 3rd day: Confusion and stupor, right hemiplegia, plantar reflex extensor on right; equivocal on left. 4th day: Coma, right oculomotor palsy, quadriplegia. 6th day: Death.

was extensor on the right and equivocal on the left. On the following day she had become comatose. It was thought that the left arm was now paralysed though the left leg still moved when pricked with a pin. The left pupil was 2 mm. and the

right 4 to 5 mm. in diameter and neither reacted to light. The right eye deviated outwards. The patient's condition grew rapidly worse. Her respirations became short and grunting, temperature rose to 106°F. and she died on the sixth day of her illness

Anatomical diagnoses.—Thrombosis of the basilar and right posterior cerebral arteries; infarction of the pons and mid-brain; atherosclerosis of the cerebral and coronary vessels; arteriosclerotic heart disease.

Pathology.—The upper two-thirds of the basilar artery was filled with a firm red thrombus which extended into the right posterior cerebral artery to a point beyond the connection with the right posterior communicating artery. The upper half of the pons and the mid-brain were pinkish-grey in colour and soft (cf. fig. 13). There was also hæmorrhagic discoloration and softening of the right calcarine cortex and of the central portion of the right optic thalamus. Several small organized infarcts, each less than 0·5 cm. in diameter were situated in the lenticular nuclei and the central white matter of the frontal and parietal lobes. Microscopic examination of the lesions of the pons, mid-brain, occipital lobe and thalamus revealed recent infarction as evidenced by shrunken nerve cells and shrunken, darkly stained glia-cell nuclei. In the hæmorrhagic areas there was infiltration of polymorphonuclear leucocytes. There were a few microglial phagocytes in the infarct of the occipital lobe.

Comment.—The nervousness, forgetfulness and lack of initiative may be correlated with the multiple, small, old infarcts in the cerebral hemispheres. The impairment of vision which was the earliest symptom was undoubtedly related to infarction of the calcarine cortex. The other abnormal neurological signs were explained by the pontine and mid-brain lesions.

Case 12 (A9107—M.G.H.).—Male, aged 64.

History.—The patient entered the hospital for posterior sclerectomy, cyclectomy and cyclodialysis. On the eighth post-operative day he became weak and lost consciousness for a short time. Soon afterwards his speech was slurred and he choked when he tried to swallow fluids.

Examination.—T. 101°F.; P. 90; R. 20; B.P. 195/110. When examined about twelve hours after the above-mentioned episode the patient was stuporous. There was a severe dysarthria. The pupils, which were deformed by operation, were equal in size. Visual fields and extra-ocular movements were normal. The muscles of the left side of the face were weak. The palate rose in the mid-line. There was a flaccid left hemiplegia and paresis of the right arm and leg. The tendon reflexes were more active on the left side than on the right; the abdominal reflexes were absent and there was an extensor plantar reflex bilaterally.

Laboratory data.—Urine was normal except for a 1+ positive test for sugar. Fasting blood sugar was 90 mg. per 100 c.c. White blood cell count was 12,800 with 87 per cent. polymorphonuclear leucocytes. Hinton test was negative. Cerebrospinal fluid: pressure was 100 mm.; there were 9 lymphocytes per c.mm.; total protein was 32 mg. per 100 c.c.; spinal fluid Wassermann test negative.

Course.—During the next five days the patient became more alert but on the sixth day he was worse again and was unable to speak, or even to whisper intelligibly and could only indicate "yes" or "no" with a nod or shake of his head. Attempts to write resulted in an illegible scrawl. He was unable to swallow fluids. On the eighth day he was comatose. He still moved the right arm at times. Temperature

rose to 103°F. and a chest X-ray showed consolidation in left lower lobe of the lung. The patient died on the seventeenth post-operative day or on the ninth day after the onset of neurological symptoms.

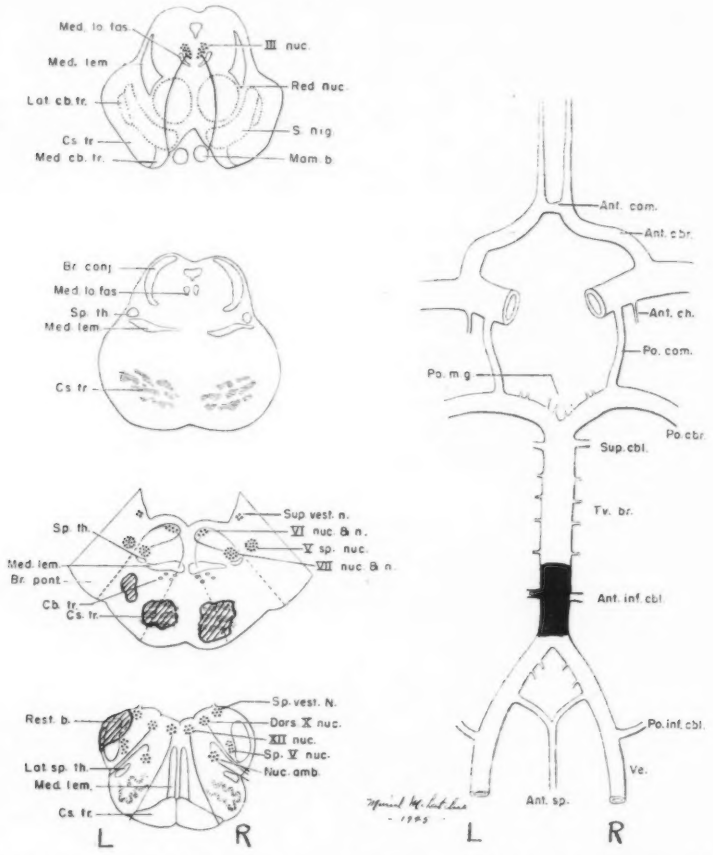

FIG. 14 (*Case* 12).—Embolism of basilar artery. Sudden onset of coma. A few hours later: Stupor, dysarthria and dysphagia, flaccid left hemiplegia, right hemiparesis, bilateral extensor plantar reflexes. 1st to 13th day: Slight improvement. 14th day: Exacerbation with anarthria, and inability to swallow. 16th day: Coma. 17th day: Death.

Anatomical diagnoses.—Embolism of basilar artery; infarction of pons and medulla; cerebral, coronary and aortic arteriosclerosis; bronchopneumonia; pulmonary œdema; chronic vascular nephritis.

Pathology.—The cerebral arteries were only slightly atherosclerotic. There was a firm, pale, pinkish embolus filling the lower third of the basilar artery. The

lower three-fourths of the base of the pons was considerably softer than normal; there was no apparent difference between the two sides (cf. fig. 14). The mid-brain and upper pons were normal and in the medulla there was infarction of a small part of the left restiform body. There were several minute foci of old infarction in the lenticular nuclei. The mass occluding the basilar artery was composed of amorphous, hyaline material which, though it was organized, was not attached to the vessel wall and was obviously an embolus. No source for the embolus was found.

Comment.—The neurological signs in this case could be explained by the involvement of corticospinal and corticobulbar tracts bilaterally in the pons. The dysarthria and dysphagia were manifestations of a pseudobulbar palsy. It is interesting that there was stupor at the onset but no lesion above the lower three-quarters of the pons. A narrowing of the basilar artery in its mid-portion was responsible for the lodgment of the embolus proximally to the bifurcation. The softening in the medulla, situated in the lateral portion of the restiform body, was probably due to occlusion of the anterior inferior cerebellar artery.

Case 13 (A44-149—B.C.H.).—Male, aged 82.

History.—Until the day before admission the patient was as well as usual. He had had arterial hypertension for many years and was enfeebled, both mentally and physically. On the previous day he suddenly began to feel dizzy and vomited several times. He complained of being unable to see and a few hours later was found in coma by his daughter.

Examination.—T. 99°F.; P. 76; R. 18; B.P. 170/95. There had been some improvement in the mental state so that the patient could now perform simple tests. His speech was very nearly unintelligible. His tongue was clumsy and he had difficulty in swallowing. The left pupil was larger than the right and did not react to light. The left eye was turned out and did not move in any direction. The retinal arteries were sclerotic. Visual acuity and visual fields could not be tested. There was a slight weakness of the left side of the face. The right arm and leg were paralysed and flaccid. Tendon reflexes were less active on the right than on the left side. The abdominal reflexes were absent on the right and the right plantar reflex was extensor. Pin-prick was felt in all four extremities, but co-operation was too poor for satisfactory sensory examination. There was incontinence of urine.

Laboratory data.—Urine: test for albumin was 1+. Cerebrospinal fluid: initial pressure was 170 mm.; protein was 42 mg. per 100 c.c., colloidal gold reaction was normal and Wassermann test was negative. The white blood cell count was 14,000 with 82 per cent. polymorphonuclear leucocytes.

Course.—On the second hospital day the temperature rose to 101°F. and moist râles were heard over both lung bases. The patient was much less responsive. All four extremities were paralysed and plantar reflexes were extensor on both sides. There was a divergent strabismus and the pupils did not react to light. Death occurred on the third hospital day or the fourth day of the illness.

Anatomical diagnoses.—Embolism of the basilar and left posterior cerebral arteries; infarction of the mid-brain, left cerebellum, optic thalamus and occipital lobe (cf. fig. 15); generalized arteriosclerosis; arteriosclerotic heart disease; bronchopneumonia.

Pathology.—At the bifurcation of the basilar artery there was a greyish-brown mass and beyond that a dark red thrombus filled the first portion of the left posterior cerebral artery to a point beyond its junction with the posterior communicating artery. The left half of the mid-brain (cf. fig. 5 upper right, Plate XI), the

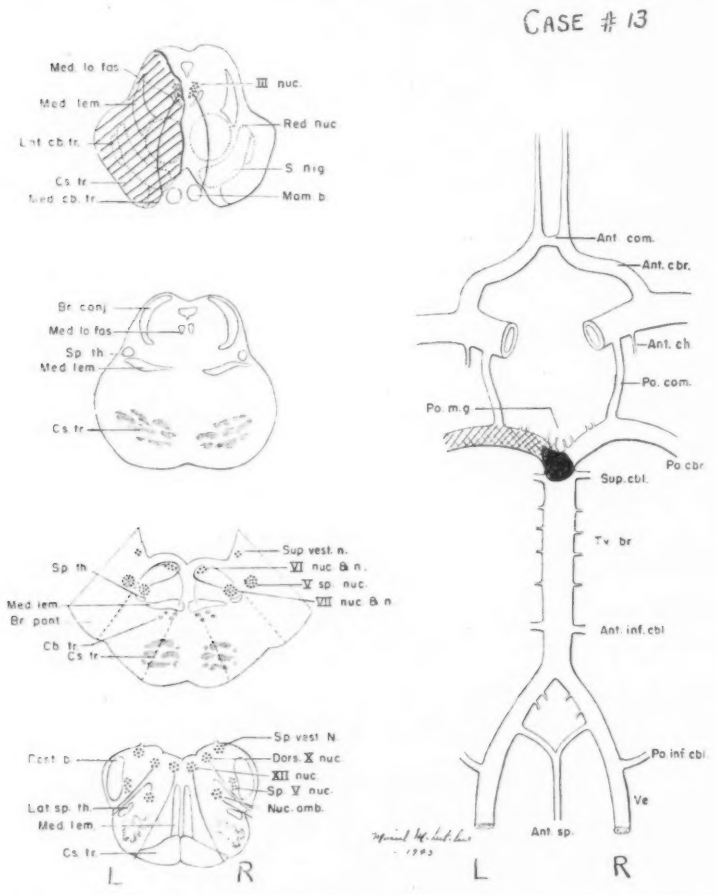

FIG. 15 (*Case* 13).—Embolism of basilar artery. Sudden onset of dizziness and vomiting, dysarthria, impaired vision. 2nd day: Coma, left third nerve paralysis, right hemiplegia, urinary incontinence, bilateral extensor plantar reflexes. 10th day: Death.

central portion of the left optic thalamus, the inferior portion of the left temporal and the medial portion of the left occiptal lobes were grey and of mushy consistence. There was a small softening in the superior portion of the left cerebellar hemis-

phere. The pons and medulla were normal. On microscopic examination the mass occluding the basilar artery proved to be an embolus.

Comment.—The embolus was lodged in the basilar and left posterior cerebral arteries thereby obstructing the blood flow to the superior portion

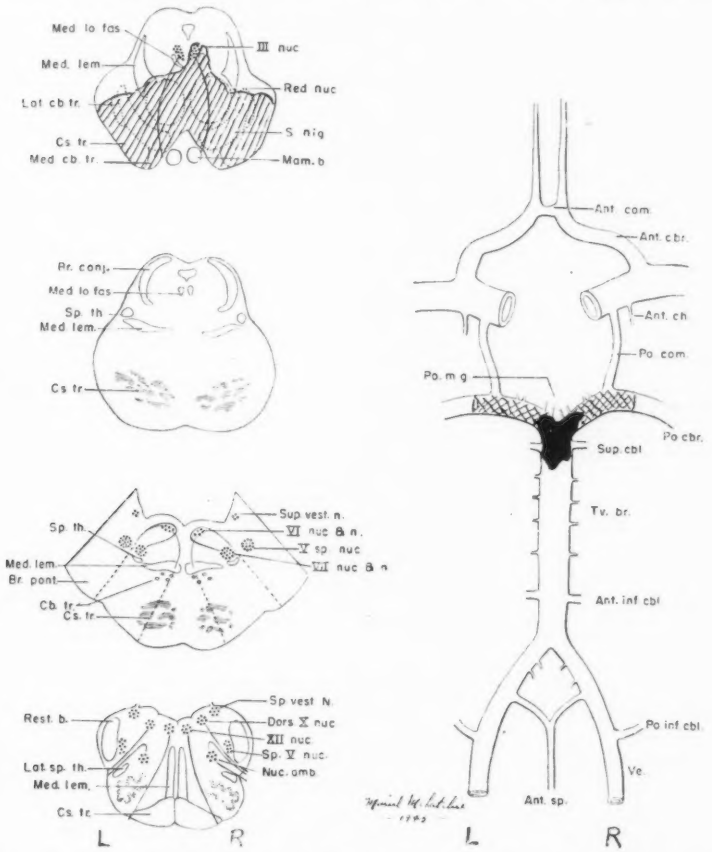

FIG. 16 (*Case* 14).—Embolism of basilar artery. Sudden onset of coma, left facial paralysis, right hemiplegia, bilateral extensor plantar reflexes. 2nd Day: Deeper coma, T. 107, death.

of the left cerebellar hemisphere and to the cerebral peduncle, optic thalamus and occipital lobe. Loss of vision at the onset was unquestionably due to involvement of calcarine cortex. The left oculomotor palsy and crossed hemiplegia was the result of infarction of the left cerebral

peduncle. The left facial weakness was probably caused by involvement of corticobulbar tracts since there was no lesion in the lower pons. The source for the embolus was probably the fibrillating left auricle even though no mural thrombi were found at autopsy.

Case 14 (A7924—M.G.H.).—Male, aged 74.

History.—An elderly man with benign hypertrophy of the prostate was admitted to the hospital for prostatectomy. Pre-operative examination revealed auricular fibrillation and slight cardiac enlargement to the left. On the seventh post-operative day he got up for the first time and a few minutes later suddenly lost consciousness.

Examination.—T. 102°F.; P. 100; R. 25; B.P. 146/100. The patient was comatose and breathing rapidly. He had a left facial paralysis and a crossed paralysis of the right arm and leg. Plantar reflexes were extensor, bilaterally. There was no record of pupillary or ocular findings.

Course.—He remained in coma and died two days later. Terminally his temperature rose to 107°F., pulse to 100 and respirations to 30.

Anatomical diagnoses.—Embolism of basilar artery; infarction of mid-brain and occipital lobe; moderate aortic and coronary arteriosclerosis; pulmonary congestion and œdema.

Pathology.—There was an embolus at the bifurcation of the basilar artery occluding the medial ganglionic, both superior cerebellar and both posterior cerebral arteries (cf. fig. 16). There was softening of the mid-brain, superior portions of both cerebellar hemispheres, the central portion of each optic thalamus and the medial portion of the left occipital lobe. The pons, medulla and right occipital lobe were not affected. The source for the embolus was not discovered.

Case 15 (A9698—M.G.H.).—Male, aged 52.

History.—The patient entered the hospital on August 13 because of an illness of two weeks' duration in which fever, malaise and anorexia had been the chief symptoms. Previous to this illness he had been quite well. A heart murmur was known to have been present for at least twenty years, but no history of rheumatic fever could be obtained.

Examination.—T. 102°F.; P. 100; R. 20; B.P. 116/64. Mental status was normal. The heart was normal in size; there was a harsh systolic murmur at the apex. Several red spots, thought to be petechiæ, were observed on the abdomen. The liver was felt 3 cm. below the costal margin.

Laboratory data.—White blood cell count was 22,200 with 85 per cent. polymorphonuclear leucocytes, the hæmoglobin was 14·1 gm. Blood culture grew *Streptococcus viridans*. Urine was normal.

Course.—On August 21 he suddenly developed ptosis of the upper lid and lateral deviation of the left eye and a right hemiplegia. He became stuporous. On August 27 he had become comatose, respirations were 64 and "gasping"; pulse was 148. Temperature rose to 104·5°F., and the patient died six days after the onset of neurological symptoms.

Anatomical diagnoses.—Embolism of basilar artery and infarction of mid-brain, left optic thalamus and both occipital lobes; subacute bacterial endocarditis, of mitral valve; active rheumatic myocarditis, embolic glomerulonephritis.

Pathology.—The distal portion of the basilar artery was filled with a firm pinkish-grey mass which extended about 3 mm. into the left posterior cerebral and 1 mm. into the right posterior cerebral artery. The medial surface of the left

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occipital lobe near the pole was soft, almost diffluent. On the cut surface of the left optic thalamus there was an area, 0·5 cm. in diameter, of brownish discoloration resembling recent infarction. The mid-brain was not definitely abnormal. Microscopic examination revealed an embolus in the occluded portion of the basilar artery and confirmed infarction of the left occipital lobe and left optic thalamus.

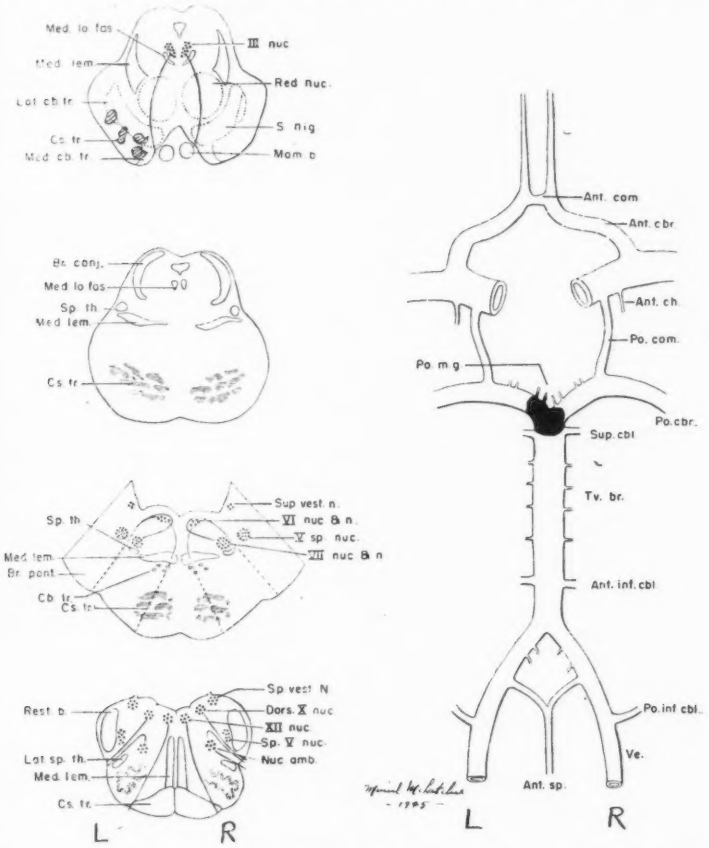

FIG. 17 (*Case* 15).—Embolism of basilar artery. Sudden onset of confusion, left oculomotor palsy, right hemiplegia. 5th day: Coma. 6th day: Death.

In the mid-brain the only abnormal finding was a small number of microglial phagocytes in the left cerebral peduncle (cf. fig. 17).

Comment.—Although there was surprisingly little pathology in the mid-brain, it seems reasonably certain, because of its location, that the embolus was responsible for the left oculomotor palsy and the right

hemiplegia. It seems likely that there was collateral blood supply adequate to prevent necrosis but not to maintain function.

Case 16 (10062—M.G.H.).—Male, aged 58.

History.—At 9 a.m. on June 9 the patient suddenly stopped talking, slumped in his chair and lost consciousness. At 1 p.m., when examined by his physician he was comatose, his breathing was stertorous and of Cheyne-Stokes' type, the left pupil was larger than the right and the plantar reflexes on both sides were extensor. In the past few weeks the patient had often complained of headache and of feeling tired. His weight, which was 260 lb., had been excessive since adolescence. The highest systolic blood-pressure had been 160 mm.Hg a few months before.

Examination (at 3 p.m.).—T. 99·8°F.; P. 70; R. 15 (Cheyne-Stokes'); B.P. 120/86. The patient was in a state of deep coma, making no response when spoken to or to painful stimuli. The right pupil was 2 mm. in diameter and the left 4 mm.; neither one reacted to light. The eyes were in neutral position. The left side of the face was more flushed than the right Optic fundi were normal. Although no response was elicited by pricking either arm or leg with a pin, the right hand grasped at the bedclothes several times. The tendon reflexes could not be elicited; the abdominal reflexes were absent and the plantar reflexes were extensor bilaterally. The heart was enlarged to the left and there was a loud systolic murmur over the base which was transmitted to the neck, and over the apex.

Laboratory data.—The urine gave a 1+ test for sugar and was otherwise normal. The red blood count and hæmoglobin were normal; the white blood count was 9,200 with 74 per cent. polymorphonuclear cells. The cerebrospinal fluid pressure was 220 mm.; the total protein was 73 mg. per 100 c.c.; colloidal gold 1122100000; Wassermann test was negative.

Course.—There was slow, steady improvement and on the ninth day of the illness the patient responded occasionally to simple questions. The left upper eyelid drooped. There was weakness of the left side of the face and the right arm and leg. The plantar reflex was extensor on the right and equivocal on the left. On the tenth day of the illness the patient became comatose and his temperature rose to 103°F. On the thirteenth day he improved again to the point where he recognized his wife and followed her about the room with his eyes and at times even talked a little. He remained incontinent of urine. Much of the time both day and night, he was asleep, and when aroused he was confused and incoherent. The pupillary inequality and the weakness of the right arm and leg persisted but the left plantar reflex became normal. On July 11 râles were heard in both lungs, temperature gradually rose to 106°F. and death occurred on July 12, which was the thirty-fifth day of the illness.

An electroencephalogram was done on June 18, 1944, at a time when the patient was semicomatose; slow (3, 4 and 5 per second) waves were obtained from both hemispheres.

Anatomical diagnosis.—Embolism of the basilar artery; infarction of mid-brain and optic thalami; calcific aortic stenosis; congenital heart disease—bicuspid aortic valve; subacute bacterial endocarditis, non-hæmolytic streptococcus; splenic infarction; bronchopneumonia.

Pathology.—There was a sharply defined focus of hæmorrhagic discoloration in the mid-brain (cf. fig. 18 and lower left of fig. 5, Plate XI). The left mammillary body was greyish-brown in colour and soft. In the central part of each optic thalamus there was a round, poorly demarcated greyish-pink lesion about 1 cm. in diameter.

Nothing abnormal was seen in the occipital lobes, pons, cerebellum or medulla. The basilar artery contained a fresh post-mortem clot. In microscopic sections there was a lymphocytic infiltration in the wall of the upper part of the basilar artery. The lesions in the mid-brain, optic thalami, and mammillary body were of approximately the same age and consistent in appearance with infarction one month old.

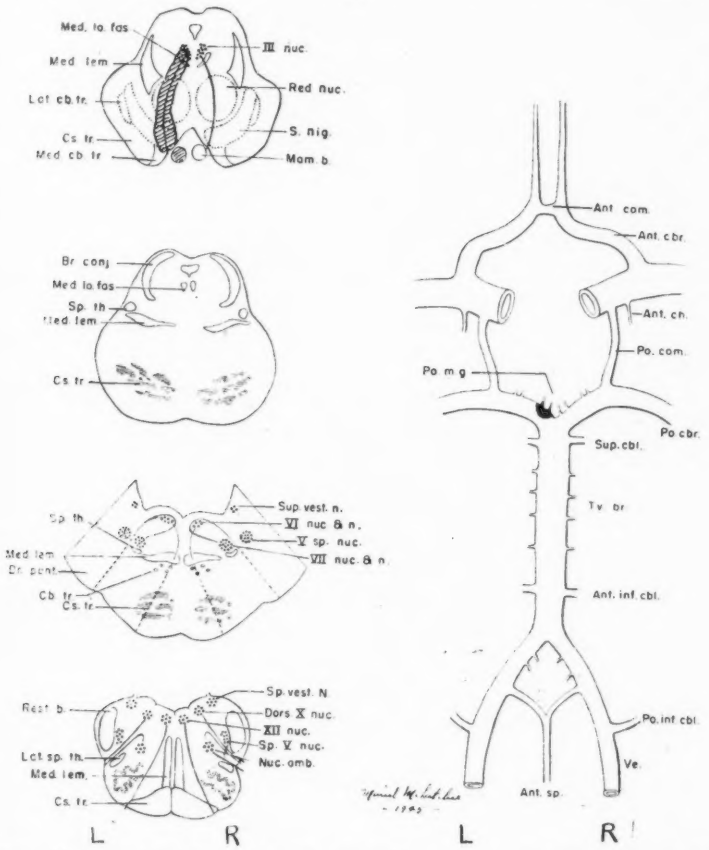

FIG. 18 (*Case* 16).—Embolism of the basilar artery. Sudden onset of coma, dilated left pupil, bilateral extensor plantar reflexes. 2nd—9th day: Improvement, now stuporous, left third nerve paralysis, left facial weakness, right hemiparesis, urinary incontinence. 10th day: Coma, T. 103. 11th to 34th day: Improvement, still drowsy and confused, left third nerve paralysis, right hemiparesis. 35th day: T. 106, death.

Comment.—In this case there was probably a shower of small emboli which simultaneously occluded medial ganglionic branches of the upper

basilar and posterior cerebral arteries and thalamic branches of both posterior cerebral arteries. The emboli, presumably because they were too small, were not found, but the lymphocytic infiltration of the wall of the basilar artery indicated that it had recently been the site of a pathological process. The terminal events of the illness were probably due to infection rather than fresh vascular lesions of the brain. The somnolence and coma in the case were striking symptoms and persisted throughout the course of the illness; they were presumably due to one or a combination of the lesions in the mid-brain, mammillary body and optic thalami.

Case 17 (A7573—M.G.H.).—Female, aged 58.

History.—This patient entered the hospital on December 28 because of pain in and swelling of the abdomen and loss of weight of two years' duration. Several hours after she was admitted 5,000 c.c. of amber-coloured fluid were removed from the abdomen by paracentesis. On the following day she suddenly became comatose.

Examination (Shortly after onset of coma).—T. 98° F.; P. 80; R. 20; B.P. 144/85. The patient was in deep coma, making no response to painful stimuli. Breathing was stertorous. There was a left hemiplegia affecting the face, arm and leg. Plantar reflex was extensor on the left and normal on the right side. There was a mass in the lower abdomen

Laboratory data.—Urine: test for albumen was 1+. White blood cells were 13,000 per c.mm.

Course.—Temperature rose to 105° F., pulse to 120, and respirations to 40. Death occurred on December 31, two days after the onset of coma.

Anatomical diagnoses.—Embolism of basilar artery; infarction of the pons; peritoneal carcinomatosis, probably primary in the right ovary, with metastases to the lung.

Pathology.—The mid-portion of the basilar artery considerably narrowed and was filled with a white firm embolus, 1 cm. long, which on microscopic examination consisted of degenerate tumour, presumably derived from invasion of a pulmonary vein by metastatic carcinoma (cf. fig. 19). There was a dark red thrombus above and below the embolus as illustrated.

Comment.—Although there was infarction of both sides of the pons the clinical record only reported a left hemiplegia, but the patient was deeply comatose and it is quite possible that a partial paralysis of the right side could have been overlooked. A tumour embolus large enough to be seen with the naked eye is a rare occurrence in our experience. This case illustrates how a thrombus may form proximally and distally to an embolus.

Case 18 (A10907—M.G.H.).—Female, aged 32.

History.—This housewife, delivered two months before of her third child after a "toxic pregnancy," began to complain of a severe, steady frontal and occipital headache, nausea and vomiting. These symptoms had been present two days when she went to a drug store to telephone her physician, but was too weak and ill to

walk back to her home. She was taken home in an automobile and two and a half hours later was found by her husband lying across her bed fully clothed, unconscious and covered with vomitus. She was immediately taken to a local hospital where during the next twenty hours she remained in the same comatose state. Her pulse at that time was 70, blood-pressure 138/52, respirations 17 and temperature 99°F. Her right arm and leg were paralysed. The left arm and leg were moved aimlessly.

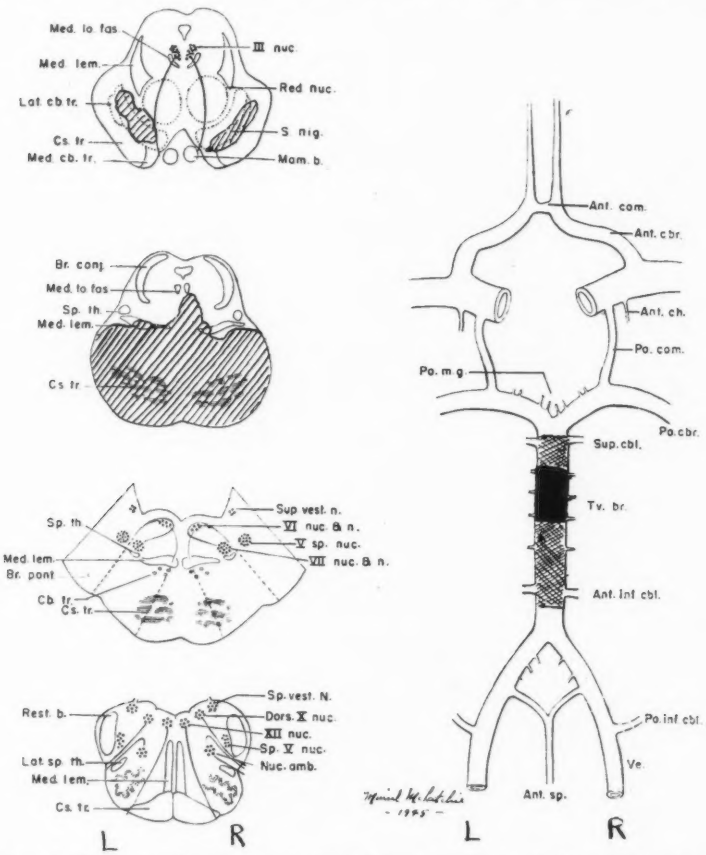

FIG. 19 (*Case* 17).—Tumour embolism of basilar artery. Sudden onset of coma, left hemiplegia. 2nd day: Death.

The tendon reflexes were less active on the right side than on the left and the right plantar reflex was extensor. She was then sent to the Massachusetts General Hospital.

For the preceding nine years the patient had been subject to severe recurrent generalized headaches, accompanied by dizziness and at times by nausea and vomit-

ing. These headaches had been more frequent and severe during and after the last pregnancy when she was said to have had hypertension and œdema of the ankles.

Examination (8 a.m. August 11).—T. 101°F.; P. 90; R. 20; B.P. 120/80. At this

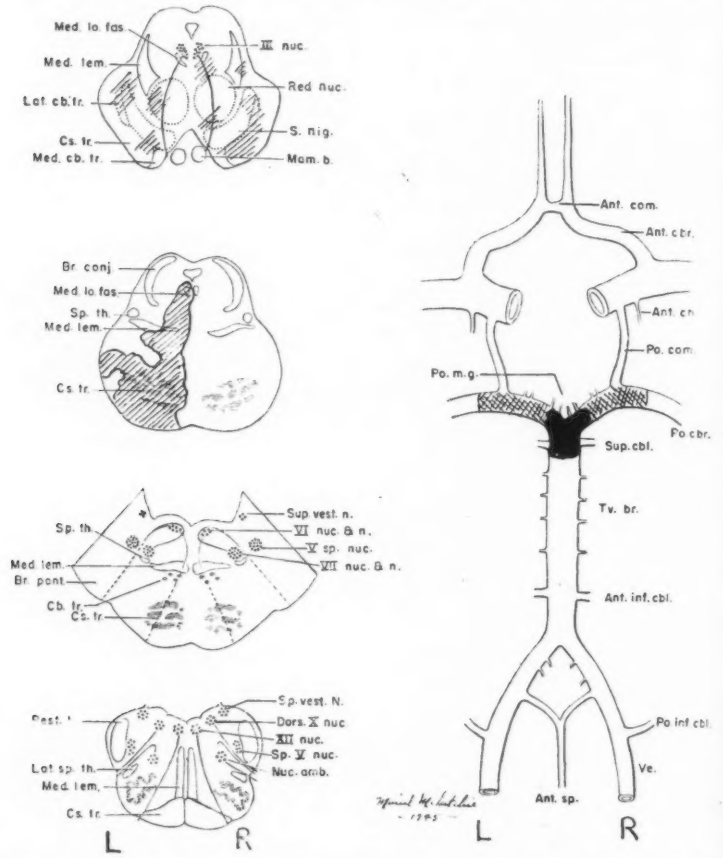

FIG. 20 (*Case* 18).—Embolism of basilar artery. Acute onset of occipital headache: nausea and vomiting. 3rd day: Coma, right hemiplegia. 4th day: Coma, dilated, fixed pupils, eyes deviated to right, bilateral extensor plantar reflexes. 7th day: cyanosis, T. 102·5, death.

time the patient was comatose. The left arm and leg were withdrawn from painful stimuli, but the right arm and leg, which were inert and flaccid, were not. Both pupils were dilated and did not react to light. The eyes tended to deviate to the right. The tendon reflexes were diminished on the right side and the plantar reflexes were extensor bilaterally.

Laboratory data.—Cerebrospinal fluid obtained on the first day of the illness was under a pressure of 140; it was clear and contained no cells. White blood count was 9,000 with 90 per cent. polymorphonuclear leucocytes. Urine was normal. NPN was 53 mg., CO_2 combining power was 43 vol. and sugar 110 mg. per 100 c.c.

Course in the hospital.—Because of the long history of headaches the possibility of a subdural hæmatoma was considered and bilateral temporal burr hole explorations were made and were negative. For the next two days the patient remained in the same condition. She became cyanotic, her temperature rose to 102·5°F. and pulse to 130. She died at 11.30 p.m. on August 13, four days after the onset of coma.

Anatomical diagnoses.—Embolism basilar artery; infarction of pons, mid-brain, optic thalami, occipital and temporal lobes and superior cerebellum

Pathology.—There was little if any arteriosclerosis. Beginning at the level of the superior cerebellar arteries the basilar artery was distended by a hard, dark purplish red and grey mass which had the appearance of an embolus. Dark purplish clot extended into and distended both posterior cerebral arteries, for some distance beyond the posterior communicating arteries. There was softening of the medial and inferior surfaces of both occipital lobes, inferior surfaces of both temporal lobes, both optic thalami, and the base of the pons (cf. fig. 20 and lower upper right of fig. 5, Plate XI). The lesions of the optic thalami were pale, mushy and granular; those of the occipital and temporal lobes were mottled pale and hæmorrhagic and appeared to be more recent than those of the optic thalami.

Microscopically the occluded portion of the basilar artery was filled and distended by two types of blood clot; in one there was beginning organization and polymorphonuclear infiltration; the other was more recent. The findings presumably represented embolism with superimposed thrombosis. There were some red blood cells and small amounts of patchy subarachnoid exudate, composed of polymorphonuclear cells, over the medulla and portions of the cerebrum. In the base of the pons, cerebellum, occipital lobes and optic thalami there was infarction. Some of this was not accompanied by any microglial reaction and appeared to be twenty-four to thirty-six hours old. In other regions in which there was a fair number of microglial phagocytes the lesion was probably three or four days old.

Comment.—Although the autopsy was restricted to the head and the diagnosis could not be definitely established the findings were suggestive of a bacterial endocarditis and that might raise the question of multiple emboli but, since all the regions of infarction were supplied by branches of the occluded portion of the basilar artery, it would seem likely that this alone was responsible for the infarction.

Discussion.

I. *The blood supply of the pons and mid-brain.*—The pons is supplied with blood by the basilar artery and the mid-brain by the basilar and posterior cerebral arteries. The branches of the basilar artery have been divided into three groups by Foix and Hillemand: (1) Paramedian branches; (2) the short circumferential; and (3) the long circumferential see fig. 21, Plate XII). The following description summarizes their views and is in agreement with our own observations.

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The *paramedian arteries* which are also known as the median arteries of Duret are usually 3 to 5 in number and branch from the posterior surface of the basilar artery to enter the pons just a few millimetres lateral to the mid-line. They divide immediately into small arteries which run perpendicularly to the long axis of the pons. As shown in fig. 22 (Plate) they supply a territory which is limited to the medial portion of the base of the pons and to the most ventral part of the tegmentum. The corticospinal and corticobulbar tracts, pontine nuclei and ponto-cerebellar fibres and part of the median lemniscus are situated within this territory. In the lower part of the pons the fibres of the abducens nerves traverse this field. Corresponding to the paramedian arteries are the *medial ganglionic arteries* which arise from the bifurcation of the basilar artery and enter the posterior perforated space to supply the medial portions of the cerebral peduncles and the red nuclei.

The *short circumferential branches* arise from the more lateral part of the wall of the basilar artery. These arteries, 4 or 5 in number and longer than the paramedian branches, pass laterally for a distance of nearly 1 cm. before entering the pons. They supply the lateral three-fifths of the pons, a territory which includes some of the pontine nuclei, the lateral parts of the corticospinal tract and median lemniscus, the trigeminal and facial nuclei and the middle cerebellar peduncle. The corresponding lateral parts of the mid-brain, including the major portion of the cerebral peduncle, receive branches from the posterior cerebral artery.

The *long circumferential arteries* are 2 in number, the superior cerebellar and the *middle* or *anterior inferior cerebellar* arteries. These vessels branch from the lateral wall of the basilar artery and course around the brain-stem to reach the cerebellum. As they do so several small branches to the lateral tegmentum and tectum are given off. These latter branches supply a region which includes the lateral spinothalamic tract, spinal nucleus and tract of the trigeminal nerve, cochlear and facial nuclei, the spinocerebellar tracts and superior cerebellar peduncles (cf. fig. 23, Plate XIII).

Our knowledge of the vascular supply to the tegmentum of the pons and mid-brain is still uncertain. There is so much overlap of collateral vessels that injection techniques have not settled the problem. It seems clear that the paramedian vessels supply only the ventromedian part and that the long circumferential vessels supply the lateral part. It might be deduced from this that the portion between is supplied by the short circumferential arteries. Foix and Hillemand concluded that the superior

cerebellar arteries provide for the tegmentum and tectum of the mid-brain and that the short circumferential arteries do so for the pons. In our material we have not found the medial part of the tegmentum affected in occlusions of the superior or anterior inferior cerebellar arteries and are therefore inclined to believe that most of the tegmentum of the pons is supplied by short circumferential arteries with a variable collateral circulation coming from the paramedian and long circumferential branches. The posterior ganglionic branches given off from the bifurcation of the basilar artery and from the first portions of posterior cerebral arteries supply the tegmentum of mid-brain (cf. fig. 24, upper right of Plate XIII).

It was found that the position and extent of the occlusion determined the form and size of the infarct. Frequently, as judged from the symptoms and clinical findings and from the location of the oldest part of the softening, a thrombus first occluded a paramedian or short circumferential branch or branches and later extended into or filled the basilar artery. If the posterior communicating arteries were of good size, a thrombus limited to a part of the basilar artery would only affect the circulation of the branches actually blocked off by it. If a cerebellar artery (long circumferential) became obstructed there was usually infarction of the part of the cerebellum supplied by it, but this did not always happen, presumably because of collateral blood supply from the posterior cerebral and the other cerebellar arteries. If the thrombus or embolus extended into the posterior cerebral artery, the branches to the thalamus and those to the cerebral peduncles were blocked off. As a rule when the occlusion extended beyond the junction with the posterior communicating arteries or when the latter were abnormally small there was infarction of the posterior and inferior parts of the temporal and the inferior, median and posterior parts of occipital lobes, and occasionally of the posterior and inferior parts of the temporal lobes.

II. *Symptomatology.*—The clinical features of thrombosis and embolism differ in only minor details and may therefore be discussed together.

The bare clinical aspect, divested of minute details may be epitomized as follows: The onset is sudden and not preceded by tangible causal factors. The first symptom is usually headache, "dizziness," confusion or coma. Difficulty in speaking and unilateral paræsthesias occur in a large proportion of the cases. Common findings are pupillary abnormalities, disorder of ocular movements, facial palsy, hemiplegia, and/or quadriplegia, and bilateral extensor plantar reflexes. Cranial nerve palsies

and contralateral hemiplegia may be combined. Not all of these signs are present in every case. It is common for temporary improvement, lasting hours or days, to occur during the course of the illness. In the majority of cases death takes place in from two days to five weeks. A few cases unquestionably survive. The cerebrospinal fluid is normal.

(1) *Disturbances of consciousness* varying in degree from slight confusion to deep coma was one of the earliest and most constant symptoms: it occurred sooner or later in every case. In some of the records it was designated as "delirium," irrationality, "incoherence" or "drowsiness." In many cases (Nos. 3, 7, 12, 13, 14, 15, 16, 17), coma was an initial and often transient symptom. In some of these there was temporary improvement with partial or even complete recovery of consciousness. In one case (No. 3) there was a curious and interesting condition where the patient seemed to hear and see but was powerless to respond by either word or gesture, apparently because of pseudobulbar paralysis and quadriplegia. Coma as an initial symptom was more frequent in embolism (in all 7 cases) than in thrombosis (2 of 11 cases).

(2) *Dizziness* was an initial symptom in 6 of the 11 cases of thrombosis (Nos. 1, 3, 5, 6, 9, 11, 13). Its character was often inexactly described. In a few cases it resembled vertigo with the sensation of either subjective or objective rotation but in others the word "dizziness" was used to designate a state of confusion, general weakness or faintness. Dizziness was more frequent in thrombosis (6 of 11 cases) than in embolism (1 of 7 cases), but was never a prominent symptom. Tinnitus and vertigo occurred in 1 case (6) of thrombosis. Deafness was not observed. Vomiting occurred in 2 cases (13 and 18) of embolism.

(3) *Headache* was an early symptom in Cases 2, 4, 8 and 18 and in some cases preceded the onset of focal symptoms. That headache should have occurred was rather surprising because it is rare with thrombosis of cerebral arteries. It was a dull, steady aching pain, occipital in 2 cases, frontal in 1 case, frontal and occipital in 1 case.

(4) *Dysarthria and other pseudobulbar symptoms*: Marked dysarthria amounting in some cases to complete anarthria was one of the most frequent and impressive symptoms, being recorded in 13 of the 18 cases. At times the possibility of motor aphasia was suggested but closer examination disclosed the "paralytic" nature of the speech disorder. Other "pseudobulbar" symptoms were inability to swallow, in 3 cases, and paralysis of the tongue in several. Bilateral weakness of the facial muscles, emotional lability and even pathological laughter and crying were occasionally observed. Although dysarthria was found more frequently with

thrombosis (10 of 11 cases) than with embolism (3 of 7 cases) the early onset of coma may have prevented its detection in embolism.

(5) *Paræsthesias* were present in 4 of the 11 cases of thrombosis 1, 2, 4, 9, and were not recorded in any case of embolism. They were most often distributed over one-half the body and were variously described as tingling, sensation of pins-and-needles, or "as if the circulation had stopped." These sensations were more pronounced around the lips and in the hand and foot.

(6) *Hemiplegia or quadriplegia*, as was to be expected, was observed in every case, though not always at the onset. Even when the obvious paralysis was unilateral the plantar reflexes were nearly always extensor on both sides and in Case 1 both plantar reflexes were extensor before any paralysis of the arms or legs was apparent. Because many of the patients were in a state of stupor or coma a partial paralysis could unquestionably have been missed. It is more than likely that some degree of quadriplegia occurred more often than the recorded findings would indicate. In cases of obvious quadriplegia one side of the body was usually paralysed before the other and remained more severely affected throughout the subsequent course. In cases 5, 8, 9, 11 there was a crossed motor paralysis, i.e. ocular or facial paralysis and contralateral hemiplegia. In Cases 1 and 3 there were bilateral ocular palsies and hemiplegia.

Sphincter incontinence invariably developed even when a fairly clear state of consciousness was retained.

(7) *Pupillary abnormalities* were noted in almost all the cases. In only one case (4) was it clearly stated that the pupils were normal; in two cases (8 and 12) there were operative deformities and in two others (14 and 17) the pupillary findings had not been recorded. With thrombosis small, fixed pupils was the most common finding (Cases 1, 2, 3, 5, 7 and 10). In most cases of embolism and in 2 cases (6 and 11) of thrombosis the pupils were unequal and fixed. The dilated pupil was in many instances part of an oculomotor palsy. There was an oculomotor palsy in Cases 11, 13, 15 and 16, as indicated by divergent strabismus, ptosis and a dilated fixed pupil. In Cases 5 and 9 there was a unilateral abducens palsy with convergent strabismus. Trochlear nerve palsy, if present, was not recognized. In Case 1, there was a paralysis of lateral and upward conjugate movements of the eyes and in Case 3 questionable skew deviation was observed.

Unilateral or bilateral oculomotor paralysis was more frequent in embolism while abducens paralysis was observed only in thrombosis. These observations fit in with the pathological findings: emboli are usually

arrested at the bifurcation of the basilar artery, blocking the posterior ganglionic arteries which supply the third nerve nucleus and its fibres and rarely affecting the circulation of the base of the pons. Thrombosis, on the other hand, occurs lower in the basilar artery and is likely to affect the blood supply of the sixth nerve nucleus or nerve. Infarction of the pons also probably involves the descending sympathetic pupillodilator fibres and may explain constriction of the pupils observed in many cases.

(8) *Facial paralysis*: Pseudobulbar facial paralysis or weakness has already been mentioned. In two cases of thromboses there was unilateral facial paralysis and crossed hemiplegia corresponding to a lesion involving the facial nucleus or intramedullary portion of the facial nerve and the corticospinal tract. In two cases (14 and 16) a facial paralysis was associated with a lesion in the upper pons or mid-brain and must have been due to interruption of a corticopontine tract.

(9) *Impairment of vision* was recorded in Cases 2 and 8. In Case 2 a bilateral homonymous hemianopia with preservation of central vision was demonstrated while in Case 8 no visual field defect was demonstrated. It may be inferred from the post-mortem finding of infarction of the visual cortex that a homonymous hemianopia would have been present in Cases 1, 3, 4, 16, but the state of unconsciousness precluded examination.

(10) *Changes in respiration, temperature and pulse* usually occurred in the terminal stages of the illness. The respirations became stertorous, rapid and periodic or Cheyne-Stokes in type. Extreme degrees of tachypnœa up to 60 and 70 per minute were recorded in 2 cases. Temperatures of 104 to 108° F. and tachycardia as high as 160 per minute were recorded in several cases. Hyperthermia as a terminal event occurred in all cases of embolism and in 7 of 11 cases of thrombosis. In some cases signs of bronchopneumonia developed after death.

Chief Differences Between Thrombosis and Embolism of Basilar Artery.

As a rule embolism produced a more sudden and dramatic onset of symptoms than thrombosis. In some cases of thrombosis focal symptoms were preceded by headache and/or dizziness. Loss of consciousness was the first event in all cases of embolism and in only 2 of the cases of thrombosis. Unilateral or bilateral oculomotor palsy was more frequent in embolism (cf. above, under pupillary abnormalities). Abducens palsy, dizziness, headache and paræsthesias were observed only in thrombosis. Favouring the diagnosis of embolism are indications of a possible source of emboli in the heart and signs of embolism elsewhere. Except in Case 16 where the patient lived for thirty-five days, death occurred somewhat more quickly with embolism than with thrombosis.

Diagnosis.

The onset is abrupt, frequently with loss of consciousness and with signs indicating a lesion in the mid-brain and/or pons. In the majority of cases there was evidence of bilateral involvement. Outstanding features are various combinations of (1) pupillary disturbances; (2) ocular palsies and other cranial nerve palsies; (3) dysarthria; (4) bilateral extensor plantar reflexes; (5) hemiplegia, quadriplegia; (6) commonly a marked remission of symptoms which is usually temporary but may occasionally end in recovery.

Occlusion of the basilar artery is most likely to be confused with pontine or cerebral hæmorrhage, or with extensive infarction of the cerebrum. In these conditions their "vascular" character is revealed by the sudden onset. Hæmorrhage is almost invariably associated with hypertension. In our cases of pontine hæmorrhage there was a sudden onset of severe headache and vomiting quickly followed by deep coma which persisted until death. As in infarction of the brain-stem small pupils, cranial nerve palsies, hemiplegia, quadriplegia, and bilateral extensor plantar reflexes were commonly observed. The cerebrospinal fluid contained blood and was under increased pressure. Death occurred in from fifty-five minutes to ten hours. The rapidly progressive course, the sanguineous cerebrospinal fluid, and the fatal termination are the most important distinguishing features.

In massive cerebral hæmorrhage, as in many cases of occlusion of the basilar artery, there is likely to be sudden or rapid loss of consciousness and the pupils may be constricted, dilated or unequal and fixed to light. And, furthermore, there are often bilateral extensor plantar reflexes in addition to an obvious hemiplegia. The most reliable points of difference are the steadily progressive course, the deeper coma and as a rule bloody cerebrospinal fluid under increased pressure in cerebral hæmorrhage as contrasted with the tendency to partial remission, less pronounced disturbance of consciousness, less severe paralysis of the extremities, and clear cerebrospinal fluid under normal pressure in occlusion of the basilar artery. The differences as a matter of fact are much more striking than might be inferred from a simple listing of the symptoms.

Massive cerebral infarction is distinguished by the absence of pupillary and ocular abnormalities and of signs pointing to a lesion in the brain-stem. Moreover the signs are strictly unilateral, and the hemiplegia is usually more complete. To be sure bilateral cerebral infarction due to multiple emboli or thromboses may cause bilateral signs.

Cases of drug intoxication and metabolic or traumatic brain disease

may sometimes simulate basilar artery occlusion. In deep coma from whatever cause bilateral extensor plantar reflexes may be present and corneal, pupillary and pharyngeal reflexes may be lost. In these conditions, history, clinical course and laboratory data will usually lead to a correct diagnosis.

Occasionally, disseminated sclerosis or so-called acute disseminated sclerosis affecting the pons and mid-brain may closely resemble pontine or mid-brain infarction. The onset of symptoms may be acute, the signs are likely to be bilateral and to indicate involvement of the corticospinal, corticobulbar and sensory tracts and of cranial nerves. The paralyses are usually less complete and the subsequent course differs materially from that of pontine or mid-brain infarction. Sooner or later the diagnosis is established by signs of widely disseminated lesions.

Pathological Considerations.

In all the cases of thrombosis there was extensive atheromatosis of the basilar and the other larger arteries of the brain. The lumina of these vessels were often narrowed in places almost to the point of occlusion. The manner in which the thrombus developed was not often determined. An insufficient number of sections was made in most cases to permit reconstruction of the process.

Thrombosis of the basilar artery could usually be recognized at a glance. The thrombosed portion of the vessel was distended, firm and rigid and the thrombus could not be displaced by pressure. In cross section the thrombi varied in colour depending on their age. Those only a few days old were dark purplish red; older ones were brownish red or brick red. In some cases different parts of the thrombus were of two or more ages as judged by gross appearance and by different degrees of fibroblastic organization.

In embolism the embolus was usually lodged in the distal portion of the basilar artery where it divides into the two posterior cerebral arteries. This is because the basilar artery is of a larger diameter than the vertebral arteries although as in Case 12 the embolus may be lodged in the atheromatous, narrowed middle portion of the basilar artery. The colour of the emboli varied from dark purplish red to a pale grey or pinkish grey. They were quite firm and, as a rule, from 3 mm. to 1·0 cm. in length. Thrombus may be superimposed on the embolus distally or distally and proximally.

It has already been stated that there was pronounced atherosclerosis in every case of thrombosis. Embolism may also occur in a sclerotic artery

but the absence of atherosclerosis or of syphilitic arteritis is proof of the embolic nature of the occlusion.

The gross appearance of the softened pons and mid-brain differed in no way from that of any brain softening. The greater part of the infarcted tissues in every case was pale or "anæmic" though there were frequently small numbers of petechial hæmorrhages, usually clustered in the margin of the lesion and particularly in the grey matter. Swelling and palpable softness were the only other signs of very recent infarction. After five to seven days the infarcted tissue was diffluent. Microscopically the earliest changes were shrinkage and faint or deep staining of nerve cells and pyknosis of glia-cell nuclei. After twelve to twenty-four hours there was polymorphonuclear leucocytic infiltration of the hæmorrhagic regions and proliferation of capillary endothelial cells soon afterward. Microglia cells were increased in number and exhibited phagocytic activity in infarcts which were forty-eight hours old or older. In regions of necrosis nerve and glia cells were usually no longer visible in Nissl sections by the third or fourth day. At a very early stage, in less than forty-eight hours, the myelin failed to stain or stained very feebly though the myelin sheath was visible and morphologically not greatly altered. In the cases in which there was a remission of symptoms followed a few days later by a relapse, lesions in two different stages of resolution could be demonstrated histologically.

Clinical-Pathological Correlation.

Most of the clinical phenomena could be accounted for by the pathological findings. The impairment or loss of consciousness was an interesting and impressive feature of every case. It might be supposed that this could be accounted for by a lesion in the hypothalamus, subthalamus or thalamus and such a supposition would be approximately if not precisely in accordance with the observations and deductions of experimental workers (Spencer, Jackson, quoted by Penfield, 1938). In some of our cases, however, no changes in these parts of the brain could be demonstrated and in one case there was no demonstrable lesion above the lower two-thirds of the pons. Thus our findings indicate that an acute lesion of the mid-brain or pons may be capable of producing disturbances of consciousness. However the possibility of a temporary circulatory disturbance in the hypothalamus, subthalamus or thalamus cannot be excluded. A sudden circulatory insufficiency might very well cause a derangement of function without necessarily producing recognizable pathological changes. For example, sudden occlusion of the basilar artery may reduce critically the blood supply to the thalami and hypothalami. Re-establishment of an adequate

circulation through collateral channels when hæmodynamic adjustments have occurred might subsequently take place and thus account for a return of consciousness in some cases.

Dysarthria or anarthria, dysphagia and weakness of the tongue when present were unquestionably manifestations of pseudobulbar palsy, depending on bilateral involvement of the corticobulbar tracts. As shown in the diagrams these tracts are situated near the corticospinal tracts, which were damaged in every case and accounted for the paralysis of arms and legs. Paræsthesias were probably due to involvement of the medial lemniscus. Cranial nerve palsies were usually due to involvement of the infranuclear, intramedullary portion of the nerve, rather than of the nucleus. The marked changes in respiration, temperature, and pulse could not be consistently correlated with any single lesion. Thus with infarction of the mid-brain the temperatures ranged from 100° to 107° F. and with infarction limited to the pons the temperatures ranged from 99° to 108° F. It is possible that the hyperpyrexia may be accounted for in some cases by insolation of lower medullary from higher regulatory centres in the diencephalon or cerebrum.

Acute Decerebration in Humans.

Since occlusion of the basilar artery affects a virtual transection of the pons and mid-brain these cases afforded an opportunity to observe the results of acute decerebration in humans. In every case, as already stated, there was sooner or later profound derangement of cerebral function in the form of deep coma. Release of postural reflexes, as observed by Sherrington, and tonic neck reflexes of the type described by Magnus and de Klejn were not observed in 3 of the cases examined by one of us. In Case 3 several brief spasms of extensor muscles, or "tonic fits," were witnessed but the limbs were flaccid at all other times. There are two possible explanations of the absence of decerebrate rigidity in these cases. The first and most likely one is that the reflex arc, on which these postural mechanisms depend, has been interrupted: the second that some condition comparable to "spinal shock" has occurred. Certainly in most of the reported cases of decerebrate rigidity the brain-stem lesions have been chronic (cf. Magnus and de Kleijn, 1915; Wilson, 1920; Walshe, 1923). Thus it may be that only in chronic human brain-stem lesions, after the effects of spinal shock have receded, does decerebrate rigidity appear. This is in contrast to lower vertebrates where spinal shock is evanescent and extensor rigidity develops promptly after decerebration. An analogous situation led

in the past to a misunderstanding of spinal cord function. Bastian pointed out that immediately following transection of the human spinal cord all motor, reflex, and sensory functions were abolished below the lesion (Bastian's Law). Not until the work of Head and Riddoch was it fully appreciated that chronic transection of the human spinal cord induced spasticity, hyperactive tendon reflexes and mass reflexes and that the initial depression of these reflexes was a "shock effect."

Recovery in Occlusion of Basilar Artery.

It should not be supposed that thrombosis and embolism of the basilar artery are inevitably fatal. While this report was being prepared we have had under observation 7 patients whose symptoms resembled those of the above cases so closely that one could be almost certain of the diagnosis, and who are alive two to fourteen months later.

Case 19.—Male, aged 54.

History.—On the morning of October 3, 1944, the patient was dizzy and had a headache. Later while shaving the left side of his body became numb and weak. During the next few days these symptoms subsided and on October 12 he again had a headache, was dizzy and vomited. After this episode he was quite weak and had double vision, swaying and unsteadiness of gait, slurred speech, difficulty in swallowing and uncontrollable outbursts of laughter and crying.

Except for high blood-pressure of five years' duration the patient had been in good health.

Examination (October 19, 1944).—T. 99°F.: P. 80; R. 18; B.P. 180/110. The patient was almost incapable of describing his symptoms because of frequently bursting into tears. His speech was poorly articulated and when crying or laughing it became unintelligible. The retinal arteries were irregularly narrowed and tortuous. Visual fields were normal. The right pupil was 4 mm. and the left 3 mm. in diameter and both reacted to light and on convergence. The right eye turned inwards and there were a paralysis of lateral conjugate movement to the right and vertical and lateral nystagmus. The right side of the face and the left arm and leg were weak, and there was ataxia of the left arm and leg. The tendon reflexes were more active on the left side; abdominal reflexes were absent and plantar reflexes were extensor bilaterally. Sensations of vibration and position were impaired over the left side of the body.

Laboratory data.—Cerebrospinal fluid was under normal pressure and contained no cells; the total protein was 28 mg. per 100 c.c. and the Wassermann test was negative.

Course.—The patient's condition remained much the same for the next three weeks. Then he began to improve and in January, 1945, was able to do light work. When last seen in August, 1945, he was still emotionally labile. Although working he was unable to assume responsibility or to make independent decisions. He was dysarthric. The pupils were equal and the eyes were well centred. Ocular movements were normal and there was no nystagmus. The jaw-jerk was hyperactive. There was a spastic weakness of the left arm and leg. The reflexes were hyperactive on the left side of the body and the left plantar reflex was extensor.

Comment.—The dysarthria, dysphagia and the uncontrollable laughing and crying are the usual findings in "pseudobulbar palsy" and signify interruption of the corticobulbar tracts bilaterally. The corticospinal tracts also were damaged bilaterally. That the lesion is in this case in the lower part of the pons is clearly indicated by the sixth and seventh cranial nerve paralyses on the right side. The abrupt onset of symptoms followed by improvement establishes the vascular ætiology, probably a thrombosis of the basilar artery.

Case 20.—Male, aged 65.

History.—On August 16, 1945, while sitting in a chair, the patient "felt peculiar" and immediately afterwards could not speak even though his mind was clear. His right arm and leg were paralysed. The following morning upon awakening he could not open his left eye and his vision seemed impaired. When admitted to a medical ward at the Boston City Hospital he was stuporous.

In the past the patient had been quite well except for symptoms of prostatism.

Examination.—B.P. 135/70. The patient was stuporous and responded poorly to all types of stimuli, but was able to carry out simple tests. The left pupil was 6 mm. and right 3 mm. in diameter; the left reacted poorly to light. There was ptosis of the left lid, deviation of both eyes to the left, sustained vertical nystagmus and paralysis of lateral conjugate movement to the right. Visual acuity seemed to be impaired and a right homonymous hemianopia was demonstrated. There was severe dysarthria and choking when he attempted to swallow fluids. There was a right hemiplegia affecting the lower face, arm and leg: the tendon reflexes were reduced on the right side: abdominal reflexes were absent and plantar reflexes were extensor bilaterally. Tests of sensory function were difficult. Vibratory and postural senses in the right leg were probably impaired. There was urinary and fæcal incontinence.

The heart was slightly enlarged: pulse was regular: a grade II systolic murmur was heard at the base.

Laboratory data.—Cerebrospinal fluid was entirely normal except for a total protein of 46 mg. per 100 c.c. Blood and urine were normal.

Course.—During the six weeks that the patient was observed in the hospital his condition gradually improved. He responded more quickly; his speech, though still slurred, was more intelligible; the dysphagia and the sphincter incontinence disappeared. At the time of discharge the pupillary inequality, the partial left third nerve palsy, the right hemiplegia and homonymous hemianopia persisted. When last heard of, about two and a half months after the onset of symptoms, he was in a nursing home and there had been no further change in his condition.

Comment.—One can be reasonably certain that the upper portion of the basilar and the left posterior cerebral arteries had been occluded, probably by an embolus. This would have caused infarction of the left occipital lobe (right homonymous hemianopia), the left cerebral peduncle (left third nerve paralysis and right hemiplegia), and the tegmentum of mid-brain and upper pons (paralysis of vertical and lateral conjugate movement of the eyes).

PLATE XI.

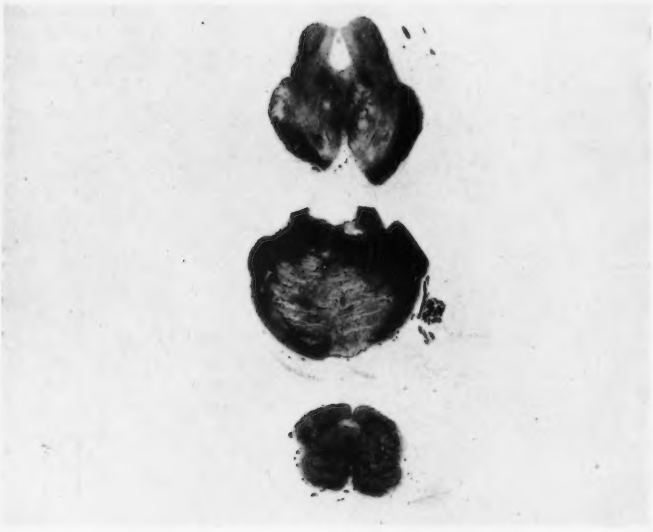


FIG. 2.

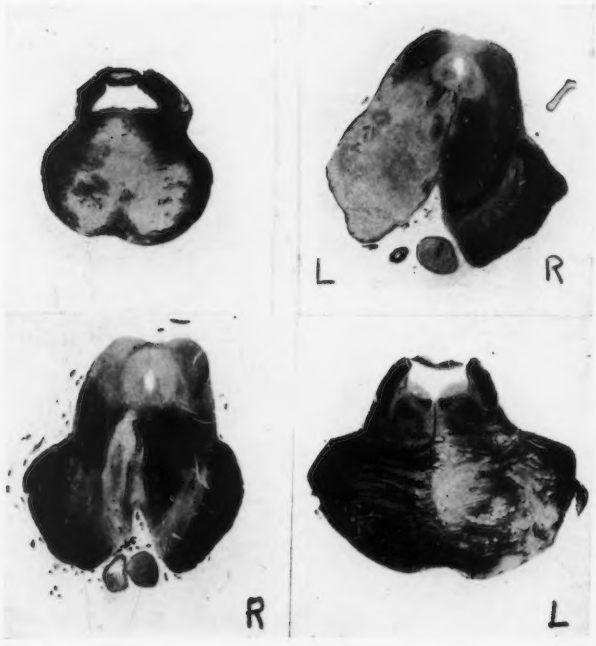


FIG 5.

To illustrate article by Charles S. Kubik and Raymond D. Adams.

PLATE XII.

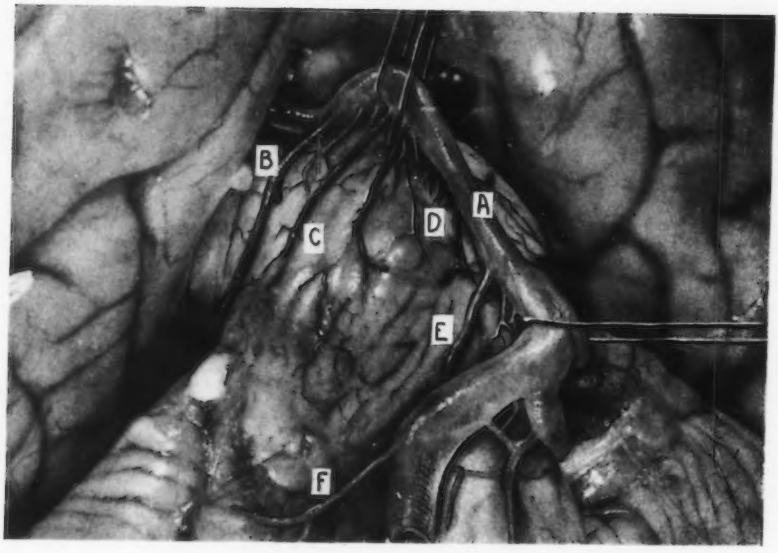
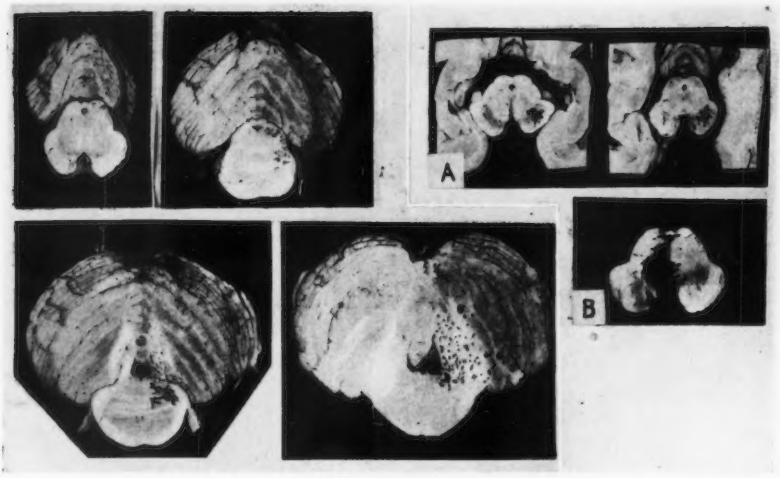


FIG. 21.

FIG. 22.

To illustrate article by Charles S. Kubik and Raymond D. Adams.

PLATE XIII.



FIGS. 23 AND 24.

LEGENDS FOR PLATES.

FIG. 2 (*Case* 1).—Photograph of sections of mid-brain, pons and medulla stained for myelin to show the foci of recent infarction.

FIG. 5, *Case* 3 (upper left), *Case* 13 (upper right), *Case* 16 (lower left), *Case* 18 (lower right).—Photographs of sections of pons and mid-brain to demonstrate degree of myelin destruction in the infarcted areas.

FIG. 21.—Photograph of the basilar artery which has been lifted by threads from the furrow in which it lies. *A*. Basilar artery. *B*. Superior cerebellar artery (long circumferential branch). *C*. Short circumferential branch. *D*. Paramedian branch. *E*. Anterior-inferior cerebellar artery (long circumferential branch).

FIG. 22.—Indian ink injection of *A* basilar artery and paramedian and short circumferential branches. *B*. Short circumferential branch. *C*. Paramedian branch.

FIG. 23.—Indian ink injection of the superior cerebellar artery (a long circumferential branch).

FIG. 24.—Indian ink injection of *A*. Small branches of the posterior cerebral artery. *B*. Paramedian or ganglionic branches.

To illustrate article by Charles S. Kubik and Raymond D. Adams.

Case 21.—Male, aged 56.

History.—An electrician was told seven months before entry to the hospital that he had hypertension. Several times in the preceding week he had felt a stinging sensation in his lips and nose and round the eyes. The day before entry he suddenly lost consciousness and fell to the floor, but picked himself up after a minute or two and drove a distance of two miles to his home. The following morning he complained of some difficulty with his vision, and of dizziness and unsteadiness. There had been no headaches.

Examination.—A slight disturbance of the state of consciousness was indicated by slowness of thought and speech, though answers were always correct and co-operation was good. Visual fields and optic discs were normal. Pupils were 3.5 mm. in diameter, equal, and reacted well to light. There was nystagmus on looking to the right or upwards and the left external rectus was paralysed. Ocular movements, including upward and downward conjugate movements, were otherwise normal. Corneal reflexes were active and sensation of the face was normal. There was very slight weakness of the left side of the face. Hearing was normal. Speech was normal or possibly slightly nasal. There was no dysphagia. The palate and tongue were normal. There was slight to moderate falling away of the extended right arm. Arm, knee and ankle jerks were more active and abdominal reflex less active on the right side; the plantar reflex was extensor on the right and flexor on the left. There was no demonstrable impairment of the sensations of light touch, pain, vibration or stereognosis, but the right leg was said to feel "numb."

Course.—On the following day there was some headache and the weakness of the right hand was more obvious. Four days after that the orbicularis oculi and frontalis on the left side were noticeably weaker than on entry. The eyes were unchanged. There was less falling away of the right arm. Plantar reflexes continued to be unchanged, extensor on the right and normal on the left. At the present time, several months later, the only residual is a partial paralysis of the left external rectus

Comment.—Paræsthesias of the face, sudden transient loss of consciousness followed by external rectus paralysis and facial weakness with signs of pyramidal tract involvement in the contralateral arm and leg leave little doubt that the lesion was in the left side of the pons or that it was an infarct, probably resulting from occlusion of a pontine branch or branches of the basilar artery by thrombosis.

Case 22 (M.G.H. unit 291128).— Male, aged 70.

History.—A lawyer had had resection of the rectum for adenocarcinoma, grade II, in 1941. Blood-pressure at that time was 190/100. On August 7, 1945, he suddenly had a feeling of light-headedness and a sensation of numbness in his lips and both arms, followed by a severe, persistent headache localized to the vertex and occiput. He then lost consciousness for a short time. There had been no weakness, diplopia, dysphagia or dysarthria.

Examination.—The patient vomited on entering the emergency ward four and a half hours after the onset of symptoms. When examined, six hours after the onset, his answers were retarded and speech was slow but there was no marked confusion and co-operation was fair. Visual fields were normal. The pupils were 3 mm. in diameter, equal and did not react to light. There was complete paralysis of upward conjugate movement above the horizontal plane. No other weakness of ocular movements was grossly apparent but examination with a red glass brought out a

slight degree of crossed diplopia on looking to either side and there were nystagmoid movements on looking to the right or left. Sensation was thought to be diminished on the left side of the face. Speech, except for being slow, was not remarkable. The patient was able to swallow water but did not slowly. The palate and tongue were normal. There was a left hemiparesis, with slight to moderate weakness of the face, marked weakness of the arm and some weakness of the leg. The arm, knee and ankle jerks were more active and abdominal reflex less active on the left side; the plantar reflex was normal on the right and questionably extensor on the left. The patient was unable to distinguish between a half-dollar and a quarter, or between a quarter and a dime with his left hand, but had no difficulty with the right. Sensations of pain and light touch were not definitely abnormal, though the left leg was said to feel abnormal subjectively.

Course.—On the following day the patient was drowsier, his neck was moderately rigid and the plantar reflex on the left side was now definitely extensor. On the sixth day there had been some improvement in strength, and astereognosis was no longer present, but drowsiness, fixed pupils, paralysis of upward conjugate movement and the reflex changes persisted. The headache stopped shortly after entry. Although he talked slowly and in a whisper, speech was fairly distinct. He had to swallow slowly but did so without choking or nasal regurgitation. On the ninth day the left eye could be moved 10 degrees to 15 degrees above the horizontal plane but upward movement of the right remained unchanged. When last heard of, several months later, the patient was able to get about in his room with assistance, but the exact neurological status was not known.

Comment.—The paralysis of upward conjugate movement, which was observed in only one of the other cases (1), and the fixed pupils indicate that the lesion was in the mid-brain. That the lesion was not limited to the tegmentum but also involved the peduncle can be deduced from the hemiplegia. Such an infarct can probably be explained by occlusion of ganglionic branches coming from the basilar artery at the point of bifurcation and the right posterior cerebral artery.

Summary.

The clinical features and pathological observations in 18 cases of occlusion of the basilar artery are described. In 11 the occlusion was thrombotic and in 7 embolic. The symptoms and signs conformed to a fairly definite pattern consisting of a change in the state of consciousness varying from confusion to coma, headache, dysarthria and dysphagia, pupillary abnormalities, ocular palsy, facial palsy, hemiplegia or quadriplegia and bilateral extensor plantar reflexes and often a terminal hyperpyrexia. The onset was abrupt, there was often temporary remission of symptoms followed in fatal cases by relapse and death. The cerebrospinal fluid was clear and under normal pressure. It should be possible in most cases of basilar artery occlusion to make a correct diagnosis. The disease is not always fatal. Histories are submitted of four patients who have recovered.

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ANOSOGNOSIA AND DISORDERS OF BODY SCHEME.

BY P. H. SANDIFER.

THE term "body scheme" was first used by Head and Holmes (1911) to signify the concept formed by the individual of his own body. It denotes the awareness that the body is an object comprising parts occupying space which are in spatial relation to each other. When this concept is disturbed by damage to one hemisphere, the subject may cease to be aware of the opposite half of his body (agnosia of body half) and often of disability involving the forgotten half of the body (anosognosia). The body scheme may be disturbed in other ways, as in Gerstmann's syndrome, but with bilateral disorders of body scheme peculiar to dominant hemisphere damage we are not concerned.

Instances of agnosia of body half and anosognosia of hemiplegia are, it is thought, sufficiently rare to warrant description of the following cases, particularly as autopsy material was available in one and also because there were sensory features peculiar to Case 1.

Case 1.—In July, 1945, a right-handed woman aged 66 was admitted to hospital for partial gastrectomy. There was a history of indigestion, recent vomiting and loss of weight. An epigastric mass was palpable and radiologically there was a large gastric ulcer which could be visualized with barium. The blood-pressure measured 255/120 and the hæmoglobin 43 per cent.

Four days later 2½ pints of blood were transfused over a period of ten hours. Ten hours afterwards she suddenly became comatose. She breathed stertorously and the left side was found to be paralysed. The blood-pressure was then 210/110 and an hour later 120/70.

Two days later the neurological findings were as follows: The patient was sleeping but easily roused. She knew she was in hospital and had come in for operation. She knew the year but was wrong in naming the month, day and date. She thought the King and Queen were George V and Mary. She could name correctly the Prime Minister. When asked how she felt she replied "fine, doctor."

She showed agnosia for the left half of her body and she was unaware of anything wrong with her left side. The conversation was as follows:

Examiner: "Give me your right hand." (Patient presented the right hand.)

Examiner: "Now give me your left hand." (Patient presented the right hand again.)

The right hand was then held.

Examiner: "Give me your left hand." Patient looked puzzled and moved neither arm.)

Examiner: "Is anything wrong with your left hand?"

Patient: "No doctor."
Examiner: "Why don't you move it then?"
Patient: "I don't know."
The left hand was then held before her eyes.
Examiner: "Is this your hand?"
Patient: "Not mine doctor."
Examiner: "Whose hand is it then?"
Patient: I suppose it is your's doctor."
Examiner: "No it is not; look at it carefully."
Patient: "It is not mine doctor."
Examiner: "Look at it—it is your hand."
Patient: "Oh, no doctor."
Examiner: "Where is your left hand then?"
Patient: "Somewhere here, I think." (Patient made groping movements near her left shoulder.)

Sensation was tested in the arms and then the legs were examined. She denied that the left leg belonged to her or that it was paralysed. The left arm was examined twice more in demonstrations to people who came into the ward. Each time the results were similar. At the third test she was temporarily convinced that her left arm was hers and that it was paralysed, but when examined a few hours later she had forgotten this. The conversation which led to the temporary dispersal of the delusion was as follows:

Examiner: "Is this your hand?"
Patient: "Not mine, doctor."
Examiner: "Yes it is. Look at that ring; whose is it?"
Patient: "That's my ring, you've got my ring, doctor."
Examiner: "No I have not. It's your hand. Look how different it is from mine." (Patient bewildered felt her left shoulder, her left upper arm and follows downward to the wrist. Then she said: "It must be my hand.")
Examiner: "And do you still say there is nothing wrong with it?"
Patient: "It seems I am wrong."

In addition to left-sided agnosia of the half-body and anosognosia of her hemiplegia she also had a left-sided hemianopia which she denied when demonstrated to her. There was also judged to be some agnosia of the left half of space as shown, however, by only one test. She was asked to grope for and find certain objects placed on a bed-table before her, the eyes being covered. She invariably failed to grope to the left, and objects on the left side were never located. Sensory testing showed no abnormality on the right side. When the left side was pricked she denied all pain. Heavy pricking of the skin and hard squeezing of the arm muscles and tendo Achillis evoked every expression of pain but denial that she felt any. The face would contort, the limbs would be withdrawn and even her speech would alter so that in a quavering voice she would deny having any pain. Joint movements were not appreciated on the left side, nor was vibration.

The retinal arteries were narrow and tortuous. The left arm was paralysed but flaccid and the tendon-jerks were unobtainable. The left leg was paralysed but slightly spastic; the tendon-jerks were increased on this side and the plantar response was extensor. All the abdominal reflexes were absent.

More elaborate investigations were planned but she died three days later before further examination was possible.

Autopsy findings were as follows: the right hemisphere bulged slightly and there was softening in a zone bounded anteriorly by the precentral sulcus, posteriorly by

the angular gyrus: above, it did not extend higher than the angular gyrus nor below, lower than the superior temporal sulcus. The maximal external softening was in the post-central gyrus.

On cutting the brain after six weeks' hardening in formalin the area of softening was seen, in coronal sections, to form a wedge fanning outwards from the thalamus to the superior temporal gyrus below and the inferior frontal gyrus above. The softening was maximal centrally and minimal peripherally. Sections through the postcentral gyrus showed a pink area about the size of a sixpence which was softer than the surrounding brain tissue, lying just below the cortex.

Histologically the vessels on both sides were thickened. The left side showed a picture of septic cerebral embolus the grosser changes being central.

Comment.—This patient showed anosognosia of a left-sided hemiplegia and of left-sided homonymous hemianopia. In addition there was neglect of space to the left side of the body and also of the left side of the body itself, for which there was complete agnosia, so that the patient denied that the left limb belonged to her. These symptoms resulted from softening in the thalamo-parietal region of the non-dominant hemisphere produced by septic embolism. The case differed in one important respect from what is usually seen in thalamo-parietal lesions of the non-dominant hemisphere. The effect of stimulating the affected half of the body is typically one characterized, not by failure of sensation (though this is usually disturbed) but by faulty localization of the stimulus. A painful impulse is, for example, experienced as painful but may be wrongly localized or even lateralized (alloæsthesia). In this case, however, all sensation was denied when the affected side was stimulated even by vigorous pricking of the skin and squeezing of deep tissues; and yet this stimulation provoked behaviour indistinguishable from that seen in a subject in excruciating pain—indeed, rather more reaction seemed to be elicited from stimulating the affected side than the normal.

The response of this patient to painful stimuli was interpreted as being a reflex, or complex of reflex actions—"sham pain" comparable to the "sham rage" of decorticate animals. Had pain been experienced as a result of stimulating parts which had passed out of consciousness the subject would, it was thought, have admitted that she felt pain but have localized it wrongly.

Woodworth and Sherrington (1904) described "pseudo-affective reflexes" simulating the expression of certain affective states in cats deprived of their hemispheres and upper part of the thalami. The motor response of Case 1 to pinching and pricking the left side of the body was unaccompanied by any change in affect and so may reasonably be termed a pseudo-affective reflex. The pathological changes in the thalamus of this case make it unlikely that this structure played any part in the nocifensor

response. Sternberg and Latzko (1903) noted that children who were hemicephalic monsters showed normal affective responses to stimulation which would be unpleasant by adult standards, even in the absence of cerebrum and mid-brain. This led Sherrington to seek "the seat of the nerve centres of mimetic expressions" outside the thalamus which Nothnagel and others had inclined to regard as the reflex centre of emotional movement.

Karpus and Kreidl (1909) studied the role of the hypothalamus in emotional expression by stimulating it electrically. They obtained sympathetic and motor responses such as occur in affective states. Bard (1928) showed that "sham rage" could be elicited not only in decorticate cats but also in those in whom all brain tissue cephalad to the hypothalamus had been removed. Masserman (1943) using an ingenious technique introduced needle electrodes into the hypothalami of cats and produced behaviour on passing a faradic current, characteristic of intense fear and rage. For reasons which include the immediate return to normal behaviour after the current was switched off, he concluded that the reaction was a pseudo-affective one unaccompanied by the appropriate emotional experience and that the hypothalamus is not "the seat of experience of affective states."

The left-sided pseudo-affective reaction of "sham pain" witnessed in this case was thought to be a complex of reflex mimetic movements mediated by an arc which did not include the thalamus, this being the site of gross pathological changes, but which perhaps included the hypothalamus.

Unawareness of disease (anosognosia) may differ greatly in degree of severity. In the milder forms there is periodic forgetting or neglect of a disability; or there may be unawareness of the existence of a disability but only till such time as it is demonstrated to the patient. Unawareness of hemianopia, neglect of half the body and of minor disabilities involving it are examples of the milder forms of anosognosia.

In contrast to this minor group, in which intellectual function is usually normal, are those patients constituting the major group. These deny their disability in the face of all proof to the contrary and there is often, if not always, co-existent intellectual defect which is commonly a confusion. Cases are to be found which are intermediate between these two groups but in all with fixed delusions that parts of the body are missing, or that gross disabilities do not exist, or with complete oblivion of half the body, definite intellectual disturbances seem always to be present.

The view has been advanced that anosognosia is due to a focal lesion interrupting pathways between the thalamus and cortex. That anosognosia of hemiplegia is due to focal brain damage is generally held, notably

by Pick (1898), Pötzl (1924). Barkman (1925), Hagen and Ives (1937), and Ives and Nielsen (1937). In the case of anosognosia of total blindness this view has been taken by Pötzl (1924), Wortis and Datner (1942), Gerstmann (1942), Olsen and Ruby (1941). The contrary view that anosognosia of total blindness is not due to focal but to diffuse cerebral damage has also been suggested. Thus Anton (1899) thought that widespread destruction of association fibres from diffuse cerebral lesions might account for denial of total blindness and Redlich and Bonvicini (1908) also considered that diffuse cerebral damage might be the cause.

That anosognosia of blindness is not always due to bilateral thalamocortical damage is shown by the existence of this syndrome in cases of blindness determined by peripheral and not central lesions. Thus Redlich and Dorsey (1945) described two patients, out of a series of six, one being blind through diabetic retinopathy and the other through optic atrophy. Both were unaware of their blindness, which was denied. Both were mentally confused. Instances of two young children are recalled from personal experience, both of whom had cerebellar tumours, secondary optic atrophy and total blindness which was not admitted. Both were of normal intelligence and were not confused. Both confabulated, one to such a degree that her mother was unaware that she was blind though she supposed her vision was poor because she continually bumped into things. In these two cases lack of insight into the blindness was ascribed, not to intellectual deterioration, but to an intellectual immaturity coupled with vivid visual imagery characteristic of childhood. The following case-record illustrates awareness of the first symptoms of a peripherally determined blindness but unawareness and denial of the final state of total blindness, which coincided with the development of Korsakow's syndrome.

Case 2.—A right-handed woman of 33 had a left occipital lobectomy performed in 1940 because it was the site of an oligodendroglioma. Thereafter she had a right homonymous hemianopia, alexia and dysgraphia.

Two and a half years later recurrence of the growth in the left temporal lobe caused a rise of intracranial pressure and some failure of vision in the remaining half-fields which was fully recognized by the patient and caused her considerable alarm. Headaches developed and she had swelling of the disc and early consecutive optic atrophy. The visual fields showed some peripheral restrictions of the left half-fields. She became unable to select named objects or to name objects presented. There was no visual or tactical object agnosia. Visual symbols, figures and letters were meaningless to her. She was unable to arrange scattered letters and figures painted on cardboard right way up but she was quite well able to arrange letters and figures cut from plywood by using her sense of touch (visual asymboly); but as with proper names in general, she could not give names to the letters or spell out words with them. Understanding of spoken speech was limited to all but fairly simple commands. On the executive side utterance was limited by the difficulty in recalling proper names. Writing was impaired for all but simple words

Thus in an attempt to write to her daughter she wrote: "Da To my dear my baby. I am in hass dy forom Mummy."

The cerebrospinal fluid was at a pressure of 280 mm. and contained one cell per c.mm. and 10 mg. of protein.

A right subtemporal decompression was performed and the dura opened. There was considerable bulging through the bone defect. She died of bronchopneumonia a month later but during the post-operative period she complained of darkness and would ask for the lights to be put on. She was completely blind but persistently and violently denied that she was. She evaded all questions about her sight whenever possible and became abusive if pressed too far. She denied not only that she had headaches but also that she had ever had headaches. She was irritable, excitable and talkative. She was disorientated in time and space. She confabulated greatly and would talk of things she imagined she could see.

At autopsy there was found a well-marked right temporal lobe hernia-cerebri. The left temporal lobe was distended by a necrotic mass of new growth, the effect of which was to dislocate the hemispheres bodily towards the bone defect on the right side, through which the right temporal lobe bulged. Because of this shift sideways the optic nerves were so stretched and under such tension that total blindness was produced.

Comment.—This case is an example of anosognosia of total blindness peripherally determined, existing in a setting of mental confusion. Before consciousness was clouded she was aware of the first symptom of visual impairment.

For anosognosia of total blindness to exist there needs to be, it seems, a degree of intellectual poverty which may be determined either by loss of functions once possessed or by intellectual immaturity. Clouding of consciousness of the kind seen in Korsakow's syndrome is a common accompaniment of anosognosia of total blindness. The same degree of intellectual poverty doubtless exists in anosognosia of hemianopia persisting as a fixed delusion, as instanced for Raney and Nielsen (1942) and probably in all forms of unshakable anosognosia and in persistent agnosia of the body-half.

Understanding of the psychology of unawareness of disease has been helped by the work of Patterson and Zangwill (1944) in their study of disorientation in the confusion-states following head-injury. They observed and sought to explain the simultaneous entertainment of incompatible belief concerning orientation. They noted limitation of the field of perception, impairment of memory retention and the influence of affect in producing the disorientation. The subject unaware of his blindness or paralysis shows many of the characteristics noted in post-traumatic confusion. Confusion is a characteristic of the gross forms of anosognosia and confabulation is a feature particularly marked in anosognosia of total blindness.

In anosognosia, as in post-traumatic confusion, a striking feature is the

entertainment of beliefs which are manifestly untenable: the claim to see yet the failure to perform acts dependent upon vision; the denial of paralysis yet the failure to move the paralysed parts; the assertion that all is well with the limbs yet the refusal to accept that the paralysed limbs belong to the body. To state that these symptoms are due to confusion is not to explain them. The restriction in perception present in the confusion following head injury exists in the patient with unshakable anosognosia who similarly tends to react to a very limited aspect of the perceptual field and finds difficulty in relating perceived objects and events to their wider settings. Such a subject also has difficulty in retaining in memory what little he has perceived. In consequence he is prevented from gaining full grasp of the new situation which he tends to regard in the way to which he has been habitually accustomed. That there is sometimes, in addition, a strong desire not to be blind or not to be paralysed is indicated by the reaction of some of these patients to attempts at convincing them of their disability. The second patient was very fearful of going blind before she finally became so and later became abusive if it were suggested that she could not see. An attitude of mind is sometimes adopted resembling that of the dysphasic in his attempt to avoid what Goldstein would call a "catastrophic reaction."

It seems likely that impaired perception and faulty memory retention inhibit cognitive mechanisms and that failure to utilize perceptual material running contrary to a strong desire, may sometimes be an additional factor in producing denial of disability. This affective element in experience has been rightly stressed by Schilder (1942) and he quotes Erwin Straus who reproached psychologists for neglecting the affective for the gnosic component of perception. It seems probable that an affective state of a negative kind producing apathy, may likewise be an element in the production of anosognosia.

That anosognosia of total blindness can result from peripheral damage to the visual apparatus, when a confusion-state co-exists, has been already shown. There seems to be no reason why anosognosia of hemiplegia may not be correspondingly produced. The following case is interpreted as being an example of such a mechanism and that unawareness of hemiplegia was the result of mental confusion.

Case 3.—A right-handed woman of 69 had a transient left-sided "stroke." Within twelve days she was back at her household duties and suffered no subsequent disability other than a tendency for the left hand to get cold easily and a very slight clumsiness of fine movements. Her husband and son knew of these sequelæ only because she had mentioned them and not because of any change noted.

Two years later she had another "stroke." Whilst putting away her purchases

after shopping, she fell and could not get up. The same day she entered hospital stuporose, speechless and paralysed down the right side.

When seen nine days later she could be roused but not enough to co-operate with anything more than a superficial examination. She failed to name most objects presented and when she did give the correct answer she perseverated thereafter. The blink reflex was absent from the right side; the right limbs were hypotonic and had diminished tendon-jerks. There was almost complete paralysis of the right arm and leg and the face was also paretic. The right plantar response was extensor. Superficial sensibility was reduced but not absent on the right. There was retinal arteriosclerosis and the blood-pressure was 190/110. She was unaware that she was paralysed then and again one week later. A fortnight afterwards she was better able to speak. She made fewer mistakes in naming objects. Her sentences were short and her style was telegrammatic. Mispronunciations were frequent and it was often difficult to understand what she said because her speech was indistinct though slow. She could obey simple commands but seldom those which entailed a choice. Reading was impossible. She could not co-operate sufficiently to manipulate cardboard letters.

When asked if she noticed anything wrong with her arms she said "yes, this one" (holding up the left hand). When asked what was wrong with it she replied "feels funny." This was taken to be her complaint of the aftermath of the stroke two years before. Asked about her right arm she said "nothing wrong with this" (pointing to the right arm). Instructed to touch nose with the left arm, she complied; but when told to do so with the right, she obeyed with the left. When the left arm was held and she was told to touch her nose with the right (indicated by tapping it) she made a movement of a few degrees. Asked again if she noticed anything wrong with the paralysed arm she replied "no." After repeated comments that she did not seem able to use it, she finally agreed . . . "I don't seem to just now." Questioned yet again fifteen minutes later whether the right arm (indicated by pointing) was quite normal, she said, "I think so. I think it is."

She was well aware that the right limbs belonged to her. There was confusion of laterality thus: when asked to point to her right eye and to her left eye she was sometimes correct and sometimes wrong. When told to present her right hand she would offer the left; when this was held she made no effort at all. There was some disturbance of colour visualization; thus when asked what a letter-box was she said "yes, put letters in." She said that the colour of a letter-box was grey. Asked the colour of a red object presented her, she replied correctly. Questioned again what colour a letter-box was, she said "grey—part of it red." She said that a banana was red and when asked if she was sure she said "red when not green." To the enquiry whether the hospital was North, South, East or West of London, she replied correctly after twenty-five seconds. The number of rooms in her house was given correctly after two trials. She numbered her fingers and toes and knew that her mouth was below her nose. She was unable to define any differences between objects such as an apple and a banana. The most important events in the recent past were unknown to her. Calculation was grossly impaired. She knew she was in hospital and that it was "a stone's throw from where I live." She knew the month but not the day or date or year.

In the right limbs all forms of superficial sensation were perceived less well than on the left. Joint position was less accurately appreciated on the right than on the left side. Two-point discrimination and tactile discrimination were impaired but not abolished on the right side, but there was no astereognosis.

The only disorder of the body scheme was a disturbance of laterality. There was no neglect of space to the right side. No hemianopia could be demonstrated after she became accessible.

The construction of a body scheme depends on the power to perceive spatial relationships between objects or parts which make up the body and also objects external to it. The ability to construct a scheme of things outside the body depends on the power to perceive spatial relations between objects which lie outside the body and objects which compose it. The localization of external objects calls for the perception of spatial relations between them and the observing body. The scheme of the body and the scheme of the world outside are interrelated, not only in the part they play in orientation but also anatomically, the nodal point being in the parietal lobe.

Various aspects of space can be thought of and there may occur selective disturbance of some of them. Brain (1941) pointed out that though external space is finally presented to consciousness as a whole, estimation of "walking distance" and "grasping distance" depends on the integrity of separate neural links; that the interruption of association paths between the visual cortex and the leg area of the post-central convolution results in disorientation of objects at a distance; while interruption of association paths from the visual cortex to the hand and arm areas leads to disorientation for objects within arm's length. It seems likely that another aspect of space, namely, that occupied by the body (personal space), is likewise subserved by a separate neural mechanism which, when interrupted, results in a disturbance of body scheme analogous to that disturbance of the scheme of the outside world which produces spatial disorientation of a kind resulting from agnosia of spatial relations. In Gerstmann's syndrome there is disability which illustrates disorientation, not for objects in external space but for objects in personal space—the objects or parts comprising the body. The finger-agnosia and inability to distinguish left from right are examples of disorientation for objects occupying personal space.

Disturbance of space-perception may be produced in ways other than by disorientation. There may exist spatial agnosia with neglect of one-half of space. Thus Brain (1941) described three patients with parietal lobe lesions, all with good topographical memory and without object agnosia. These patients, when faced with the necessity of turning to one or other side, invariably turned to the sound side and neglected that side of space opposite the lesion. Route-finding was, in consequence, grossly disturbed.

Just as there may develop disorientation in extra-personal and personal space, so, too, it is suggested there may develop agnosia of extra-personal and personal space. Nielsen (1938) described a case in which there was neglect not only of the left side of the body so that the patient would forget to dry the left half of the body after a bath, but also neglect of one side of

extra-personal space whereby in driving a car he would deviate to the left and neglect obstacles to the left. In this case there existed disturbance not only of the scheme of the body with neglect of personal space but also disturbance of the scheme of the outside world with neglect of extra-personal space. Case 1 is another example of such spatial neglect.

Agnosia of one-half of external space can sometimes be demonstrated through channels other than visual. Thus neglect of half external space may be shown by sound-locating tests. The first patient died before such tests were performed. Koch and Von Stockert (1935) described acoustic alloæsthesia in a setting of agnosia of the body-half and Parkes Weber (1942) described the case of a man with anosognosia both of left hemiplegia and total blindness who showed errors in locating the direction of sound.

The exact relationship between agnosia of space and anosognosia is uncertain, but it seems probable that neglect of one-half of extra-personal space, when associated with hemianopia involving the same side, will predispose to the neglect of this defect. Likewise that lesions producing neglect of one-half of personal space and the half of the body contained therein, when associated with ipsolateral disability, will predispose to the neglect of the half-body defect. Bilateral neglect of extra-personal space may perhaps predispose to anosognosia of total blindness.

As well as agnosia of half or part of the body, the illusion of absence of a part may also predispose to anosognosia when that part becomes paralysed. Thus in a case described by Ives and Nielsen (1937) there was an illusion of absence of the left arm which later became a delusion with denial that the paralysed arm was his. For such a delusion to develop, intellectual disturbance needs to be present. But although agnosia of the body half may predispose towards anosognosia of hemiplegia involving the forgotten limb, agnosia of a half of the body which is the site of hemiplegia, does not necessarily prevent cognizance of the hemiplegia. This is shown in a case described by Ives and Nielsen (1937). When, in addition to agnosia or illusions of absence of a paralysed part, there is clouding of consciousness, anosognosia as a fixed delusion occurs.

The physiological mechanism underlying agnosia of parts and illusions of absence of parts of the body, has often been the subject of consideration. Nielsen (1938) believed that the "essential lesion" is one which prevents sensory material necessary for the construction of a body scheme from reaching the supramarginal cortex. Deprived of this sensory material the subject's perception of the affected body-half is disturbed; but what he believes concerning his limbs, after this sense deprivation, is another matter, determined by damage outside the thalamo-parietal

projection. He may remember the affected limbs or neglect them; he may have the illusion or delusion of their absence and, if the latter, this may or may not be fixed in the face of proof to the contrary. Anosognosia of hemiplegia, he believed, is due to damage at a different site, and the pathological material so far collected, notably by Barkman (1925), points to the thalamus, isolating it from the frontal, temporal and parietal cortex. Such a lesion is thought to prevent sensation, which would otherwise indicate to the patient that his limbs are paralysed, from reaching consciousness.

If the construction and maintenance of a body-scheme depends on a free flow of sensory impulses from the body-half to the opposite supramarginal gyrus, it is difficult to see how a lesion destroying the thalamus or isolating it from the frontal, temporal and parietal lobes could fail to disturb the body scheme. Yet Nielsen claimed that such damage produces anosognosia of hemiplegia without disturbance of the body scheme. It is difficult to see in what way sensory impulses which normally provide the clue that the limbs are paralysed, differ from those which he believed necessary for maintaining a body scheme.

In contrast to the view of Nielsen and Sult (1939) that anosognosia of hemiplegia and agnosia of body-half are "different" from each other and "unassociated," is that of Meige (1914), who suggested that agnosia of hemiplegia was conditioned by agnosia of the body-half and that because the paralysed part had vanished from consciousness, disability involving these parts was not apprehended.

It is probable that anosognosia may be produced in several ways. Gross forms, it seems, may result from lesions at any level provided that there is an accompanying intellectual defect impairing judgment. Agnosia of the body-half may or may not co-exist.

One way in which minor forms of anosognosia are produced is by circumscribed lesions in the thalamocortical region. In some, at least, of these minor forms of anosognosia there is a tendency to neglect space in the way described, probably because association paths between one part of the cortex and another, are interrupted. One manifestation of this spatial neglect is amnesia of the body-half; another is amnesia of half visual space. Because of neglect of half the body and neglect of space perceived through homonymous, visual half-fields, visual and motor disturbances of the affected halves tend to be neglected.

The mechanism underlying agnosia of space, is a problem which calls for solution. The term "spatial agnosia" has been used to signify unawareness or neglect of half (or all) space outside the body or occupied

by the body. In this connection one needs to consider more carefully what is meant by the term "spatial agnosia." Spatial characteristics are essential for the construction of any scheme of the outside world. Schilder (1942) pointed out that philosophers and psychologists have regarded sensation and perception as having no spatial elements and that theories have had to be postulated to give such characteristics to experience. Schilder suggested that spatial and also temporal characteristics are necessarily inherent in every sensation and perception, even the most primitive.

If it is true that space is not merely something added to experience of the senses but is implicit in perception, then in those cases where there is neglect or forgetting of one-half of space (spatial agnosia), it is not merely space, but perception of the contents of space, for which there is agnosia. When such a perceptual disorder is produced, as must be the case, by a high-level lesion, then further damage impairing perception at a lower level, will produce effects which tend to pass unnoticed. Just as the spinal paraplegic may be oblivious of the effects of damage by pressure to his peripheral nerves below the transection level so, too, may the subject with agnosia of one-half of space be unaware of hemianopia to the same side.

Schilder draws a fundamental distinction between space filled by the body and space outside the body. Defects in perception may involve the contents of personal and extra-personal space. In the former instance agnosia occurs, not for objects and events to one side of external space but to one side of space filled by the body. One side of the body then vanishes from consciousness.

One way in which the perceptual disorder causing spatial agnosia is brought about may be by a specific memory defect of a kind which leads to faulty retention and recall of certain kinds of experience. If the ability to re-experience past events depends on the ability to form and utilize engrammatic records of current experience, then brain damage which prevents the formation and utilization of some of these records, as by interrupting association paths which link them with the rest of the brain will, when of suitable size and position, prevent the retention in memory of some forms of current experience or the evocation of some forms of past experience. It is probable that experiences of a certain class may be excluded from memory as a result of relatively circumscribed damage to association paths which are the neural links upon which these experiences depend for remembrance. Defects in memory retention for certain kinds of experience is a marked feature in spatial agnosia and anosognosia. One-half of the body or one-half of visual space then cannot consistently be borne in mind or may be entirely forgotten. It may be that this specific

forgetting and failure to learn by experience occurs because current experience meditated by distance receptors, such as homonymous half-fields, or by exteroceptors and proprioceptors of one-half of the body, cannot be recorded for any length of time. If, through more extensive damage to association paths, there is failure to recall, not only certain memories of recent but also of remote experience, then defects of a grosser kind will follow. In such an event there is failure to recall certain kinds of experience occurring before the defect developed. One instance is provided by Patterson and Zangwill (1946) who described a patient with agnosia of the left half of visual space and topographical disorientation, resulting from right parietal lobe trauma. The spatial agnosia and disorientation, they believed, was due in this particular case, to a specific loss of topographical memory.

The effects of a thalamo-parietal lesion in the non-dominant hemisphere differ from those seen in corresponding lesions of the dominant hemisphere. In the latter instance a "higher" level of function is disturbed and intellectual changes are involved over a wider field. This fact also explains why agnosia of half the body is best recognized with lesions of the non-dominant hemisphere and hence nearly always appears as a left-sided syndrome. In the dominant hemisphere activities take place, some effects of which are covered by the term "intellectual function." Study of this function shows that it is of a "higher" order than is the case with the non-dominant hemisphere; that mental processes to which the terms "symbolic thinking," "thinking by analogy" and "higher integrative thinking" have been applied, are mainly the concern of the dominant hemisphere.

And so it is that thalamo-parietal damage in the non-dominant hemisphere produces a relatively circumscribed mental defect whilst a similar lesion in the dominant hemisphere produces very much more: for in the latter instance there is so much disturbance of high-level thought processes that the agnosia of body-half cannot be distinguished or only with difficulty recognized (Brain, 1945); it is usually hidden by other and more florid symptoms. There seems to be no good reason for supposing that disturbances of the body-scheme of the kind producing agnosia of the body-half are the exclusive result of non-dominant hemisphere lesions. However, with certain lesions of the dominant hemisphere, a bilateral disturbance of the body scheme occurs—Gerstmann's syndrome.

Nielsen (1938) drew attention to the difference between the negative state of neglect or agnosia of part of the body, and the positive state in which part of the body feels as if it were absent or did not belong to its possessor. Instances have been recorded by Koch and von Stockert (1935)

amongst others. Anosognosia of hemiplegia may or may not co-exist. A patient of Ives and Nielsen (1937) volunteered that the left arm felt like someone else's "stuck on." One patient of Brain (1941) stated "all my right side feels as if it doesn't belong to me. When I move my right hand I don't feel I am moving my hand although it goes"; and another also with parietal lobe damage, described how the left side of the body sometimes felt as if it did not belong to him. In disorders of perception of this kind it would seem that the body scheme is preserved and that there is no specific memory loss of the kind which may produce agnosia of the body-half. The standard against which incoming sensory impressions are judged and compared with those remembered from the past, still persists.

The illusions of absence of unreality of part of the body experienced by these patients with parietal lobe damage, bear a striking resemblance to the symptoms of the depersonalization syndrome occurring for example, in depressive illnesses. It is possible that there is an anatomical basis common to both.

SUMMARY.

Anosognosia, it is suggested, may be produced by brain damage of two kinds—focal and diffuse. That anosognosia of blindness can result from peripheral lesions blotting out the visual fields, has been shown by Redlich and Dorsey (1945); there is always co-existing clouding of consciousness. The second patient here described is another example of anosognosia of total blindness which was peripherally determined. Anosognosia of hemiplegia unassociated with agnosia of the body-half, it is thought, may likewise result from non-specific lesions outside the thalamo-parietal segment but that there needs must be a defect of judgment such as may exist in a confusional state. The third patient is thought to illustrate such a mechanism.

It is also suggested that psychological factors underlying the delusion that disease does not exist, include defects in perception and in memory retention. The affective element in perception is thought to be another factor in the production of anosognosia. In Case 2 a strong desire not to suffer the disability which afflicted her was thought to be an additional factor in warping judgment and producing denial of blindness.

Anosognosia of blindness and of hemiplegia are believed to be predisposed by disorders of space perception. A distinction is drawn between awareness of personal space and awareness of extra-personal space. Though there may exist agnosia of both these aspects of space in the same subject, they may occur separately so that it is probable that they are

subserved by separate neural links. Interruption of association paths from the occipital and parietal cortex to other parts of the brain probably account for the impaired space perception.

Agnosia of half extra-personal space may lead to neglect not only of half-space but to neglect of inability to see the contents of half-space (anosognosia of hemianopia). Bilateral lesions producing bilateral neglect of extra-personal space are thought to predispose towards anosognosia of total blindness, a condition which exists as a fixed delusion only when mental confusion is added.

Agnosia of half personal space leads not only to neglect of its contents (the body-half) but to paralysis involving the body-half (anosognosia of hemiplegia), a condition which exists as a fixed delusion only when mental confusion is added.

Agnosia of personal and extra-personal space, it is thought, may be due to specific kinds of memory loss.

The first patient is an example both of agnosia of extra-personal space, producing anosognosia of hemianopia and of agnosia of personal space, producing agnosia of the body-half and anosognosia of hemiplegia. The delusion was fixed because mental confusion impaired judgment.

In this patient there was also an unusual response to pain stimulation which was interpreted as being a pseudo-affective reflex analogous to "sham-rage" seen in thalamic animals.

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COUGHING AND UNCONSCIOUSNESS: THE SO-CALLED LARYNGEAL EPILEPSY.

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THE association of attacks of unconsciousness with laryngeal irritation has been the subject of a number of medical communications since Charcot described two cases in 1876. The characters of the attack vary somewhat in the descriptions given by different observers but a majority are agreed upon certain features. The condition occurs almost entirely in middle-aged males of plethoric type and is often associated with laryngitis or bronchitis. The chief symptom is an attack of dizziness or loss of consciousness preceded by a tickling sensation in the larynx and a cough which is usually severe. Epileptiform movements may occur during the attack and a rather constant feature is slight mental confusion afterwards. It is usually considered that the condition is a rare one.

During an investigation into loss of consciousness among pilots and members of aircrew carried out at the Central Medical Establishment (C.M.E.) of the Royal Air Force in the years 1943 to 1945, a total of 500 cases was collected. In this series of cases were included all forms of disturbance of consciousness from the conditions of amnesia, confusion, transient giddiness or dizziness, to complete loss of consciousness with or without convulsions. No attempt was made to select the cases except that obvious examples of aural vertigo were excluded, as were cases complaining of dizziness, giddiness or loss of consciousness immediately following an accident. Apart from this the cases were collected consecutively as they attended at the C.M.E., where, sooner or later, are sent nearly all pilots or members of aircrew who are taken off flying for any prolonged period because of reasons of health. The results have been analysed and form the basis of a report to the Air Ministry.

Out of the 500 cases three had symptoms of impairment of consciousness associated with coughing.

Case 1.—An Officer Pilot aged 43 who had flown some 2,500 hours was referred to the C.M.E. because of a "fainting" attack. He joined the R.A.F. just after the

1914-1918 war and on entry gave a clear bill of health, both familial and personal. His records of sickness during service included bronchitis while in India in 1924, jaundice in 1928 and malaria in 1929 and again in 1938. He had one fairly severe crash in 1932 when he fractured his orbit and his right ankle, the latter injury causing trouble for some years. In addition he complained on various occasions of indigestion which was thought not to be due to peptic ulceration. In later years he suffered from a migrainous type of headache whch was regarded by Sir Charles Symonds as unconnected with his old injury. On entry to the R.A.F. he weighed just over 10 stone and his height was six feet. During his service the weight rose fairly steadily to a maximum of 15 stone in 1939 then settled down to 14½ stone which was the weight at the time of the attack. The blood-pressure when he joined was 115/75 and the yearly record showed little change till 1930 when both pressures showed a slight rise and for the next ten years the levels were around 130/84. A further rise then occurred and the records approximated to 140/90 which was the level at the time of the attack.

In the winter of 1944 he developed a cough which was thought to be the result of infection from his daughter who had whooping-cough. The cough was described as of a curious dry laryngeal type, starting with a tickling in the back of the throat. It was paroxysmal in character and caused considerable suffusion of the face. On three occasions he felt dizzy and "vacant" as if he were going to faint. On the last occasion he actually lost consciousness, fell to the floor and had some convulsive movements of the arms and legs.

On examination he was a man of plethoric type. Nothing abnormal was found in the heart, lungs, abdomen or central nervous system. The urine was normal. There was some congestion and swelling of the posterior part of the left vocal cord which was thought to be traumatic in origin, the result of his bouts of coughing.

The white cells numbered 5,200 per c.mm. and the differential count was, polymorphs 54 per cent., lymphocytes 36 per cent., monocytes 8 per cent. and eosinophils 2 per cent. An X-ray of the chest showed the lung fields to be clear and an X-ray of the skull showed no recent bony injury but an old injury involving the right frontal sinus. An electro-encephalogram was reported as normal.

He was kept under observation at a Chest Centre where the cause of the coughing was considered to be a pertussis infection but apart from a few slight spasms he was quite well during his stay.

No attacks of loss of consciousness have occurred since the original attack.

Case 2.—A Flying Officer Pilot aged 38 who had done over 1,000 hours flying was sent to the C.M.E. because of an attack of loss of consciousness.

He joined the R.A.F. originally in 1925 when he gave a clear family and personal history except that he had had some headaches following a minor head injury in 1918 which, however, had soon disappeared. His weight on entry was 10 st. 3 lb. and the height 5 ft. 10½ in. In 1925 he fainted for a short period when he was having his knee manipulated. He had a crash in 1927 in which he was concussed but he was back at full flying duty in two months. In 1930, following a cold, he developed acute mastoiditis for which a Schwartz operation was performed. A few weeks later, soon after his return to full duty, he was transferred to the Reserve, his weight then being just on 11 st.

He rejoined the R.A.F. at the outbreak of war. In the interim he had kept well except for an infection with filaria while doing civil work in West Africa.

On his return his weight was found to be 12 st. 8 lb. and the blood-pressure,

which had been about 120/80, was 130/84. In October, 1942, he was sent to South Africa for a course of flying training. One evening, while sitting quietly drinking a glass of beer, he laughed and some of the liquid "went down the wrong way". This caused him to choke and brought on a severe bout of coughing at the end of which he lost consciousness, was convulsed and passed water. He did not bite his tongue. He was carefully investigated in South Africa with special reference to the possibility of tapeworm infection but with negative result. The blood and cerebrospinal fluid were normal and the Wassermann reaction negative. On return to England he was again fully investigated, again with negative result. An electro-encephalogram was quite normal. After a period of observation he returned to flying duty. He was quite well for a period of two years when he relinquished his Commission and his subsequent history is unknown.

Case 3.—A Flight Lieutenant Air Gunner was sent to the C.M.E. in 1944 because of "momentary syncopal attacks." He was aged 36 and had done 450 hours flying. When he joined the R.A.F. in 1940 he gave a history of attacks of asthma if he smoked heavily; he weighed 12 st., his height was 5 ft. 11 in., and his blood-pressure 110/70. Soon after joining he fainted on parade, after being given a dose of anti-typhoid vaccine. During the next two years he was in hospital on three occasions for bronchitis. In May, 1942, he was in hospital with sciatica. It was noted at the time that he was lacking in confidence over his flying and he had a hypochondriacal outlook. Within a few weeks of returning to flying he was again in hospital with asthma. In August, 1943, his aircraft made a forced landing in the Bay of Biscay and he was again off duty for three months with a damaged ankle. During the following weeks he had considerable trouble with his asthma. In March, 1944, he gave a history that for several months he had been getting momentary attacks of dizziness while coughing or laughing so that he always had to sit down. During one of the bouts of laughing and coughing while in the mess he had lost consciousness for nearly a minute but there was no history of convulsions or of involuntary micturition. After a period of ground duty he was allowed to return to flying which was interrupted by various attacks of laryngitis. He was released from the R.A.F. in August, 1945. During his service his weight increased to 15 st. His blood-pressure which was taken over 20 times during his five years' service remained steady with readings between 110/70 and 120/85. The electro-encephalogram was quite normal.

In 2 of these 3 cases the attacks were fairly typical. The third was not so definite and there is some doubt as to whether it should be included in the group. All 3 were males and all were too heavy for their height. The ages at the time of onset of symptoms 43, 38 and 36 respectively are higher than in the general run of patients in this series, for in the 500 cases only 7 were over 40 years of age and only 10 in the 36 to 40 age-group. It is unwise to base an argument on so few cases but it does seem that the condition may not be so rare as is generally imagined when 3 cases occurred out of only 17 cases belonging to the age-groups likely to be affected. Whitty, in his search of the literature, found reports on something under 100 cases and comments that the condition is probably not excessively rare, despite

its apparent rarity in neurological literature, for most cases are referred to the laryngologist. The reason for the apparent rarity may well be that these patients do not get past the general practitioner who adopts a very reasonable "wait and see" attitude, the attack, as in the first two cases reported here, not being repeated. Many cases probably never go to a doctor at all, the attack being ascribed entirely to the cough and regarded as of no importance.

Causation of attacks.—The pathological basis of the symptoms has always been in dispute and three possible mechanisms have been suggested. Charcot thought that the symptoms were like the vertigo of Ménière's disease and in laryngological literature the condition is usually referred to as laryngeal vertigo (Thompson and Negus, 1937; Ballinger and Ballinger, 1938). The neurologist tends to regard the case as epileptic in origin and classifies it under the heading of laryngeal epilepsy (Whitty, 1943). A minority have imagined that circulatory changes due to the cough are responsible for the attack (McBride, 1884).

(1) *Laryngeal vertigo*: In the reported cases there has rarely been a history of apparent movement of motionless objects or of the patient's body in relation to surrounding fixed structures. The sole justification for retaining the name rests on the connection with Charcot's original nomenclature which seems an insufficient reason in view of the need for precision in modern terminology.

(2) *Laryngeal epilepsy*: The association of the larynx with epilepsy is most likely to be the result of one of two phenomena; either the local effect may be an aura of true cryptogenic epilepsy, or irritation in the larynx may be the appropriate stimulus causing an attack of reflex epilepsy. In a number of the reported cases the cough was not severe or was only slight and it seems more than possible that in some instances the laryngeal symptoms formed the aura of an attack of epilepsy. In other cases the symptom-complex fits closely to the definition of reflex epilepsy where attacks "follow some definite precipitating factor, usually in the nature of a sensory stimulus" (Critchley, 1933). In one case quoted by Sommerbrödt (1876) the removal of a local laryngeal growth resulted in cessation of the convulsive attacks. Critchley in his review of the subject does not mention the larynx as a factor in the production of attacks of reflex epilepsy and only incidentally refers to coughing as a stimulus in the case reported by Féré. In this case an elderly man who had suffered from a stroke was left with an extraordinary degree of reflex excitability and coughing was

one of the least of the many stimuli which would produce spasmodic movements of the left arm.

Reflex epilepsy is uncommon, some observers even doubting whether the condition exists, and it would seem to be a diagnosis which should rarely be made.

The electro-encephalogram has been done on an insufficient number of occasions in these cases to afford much help and probably the only reported instances are in two of Whitty's patients and in the three noted here. In only one of these 5 cases—Whitty's case No. 3—was there an abnormal electro-encephalogram and here the record was suggestive of epilepsy.

Even if it were correct that the laryngeal effect is an aura, or that some cases are examples of reflex epilepsy, is this sufficient justification for regarding the condition as a separate syndrome?

To sum up, while certain of the cases are primarily neurogenic, in others, in which the attack or attacks are associated only with severe coughing, the grounds on which an epileptic basis is postulated are not convincing.

(3) *The cardiovascular theory*: The possibility that the mechanical or chemical effects caused by coughing might be sufficient to produce the symptoms has been considered by various observers but has usually been rejected or ascribed to factors, such as cardiac asystole, of which there is no objective evidence. It is obvious from the description of the symptoms that cerebral anæmia plays no part, for the state of the cerebral circulation at the time of the attack is the antithesis of this condition.

It is remarkable, considering the commonness of coughing, how little attention has been given in medical literature to what may be described as the physiology of the symptom. Hamilton, Woodbury and Harper (1944) studied the effect of coughing on the arterial, cerebrospinal and venous pressures in man by means of a differential manometer. They suggest that during coughing the strain is taken by the peripheral arterial system while the vital arteries are protected in some way. This is hardly in consonance with the clinical evidence and fails to explain the well-known occurrence of hæmorrhage within the cranial cavity as a complication of whooping-cough. It seems more likely that the cerebral vascular changes as with "the cardiac and respiratory variations in cerebrospinal pressure are of considerably greater magnitude than is generally realized" (O'Connell, 1943).

The effects of a single bout of coughing on the other bodily mechanisms,

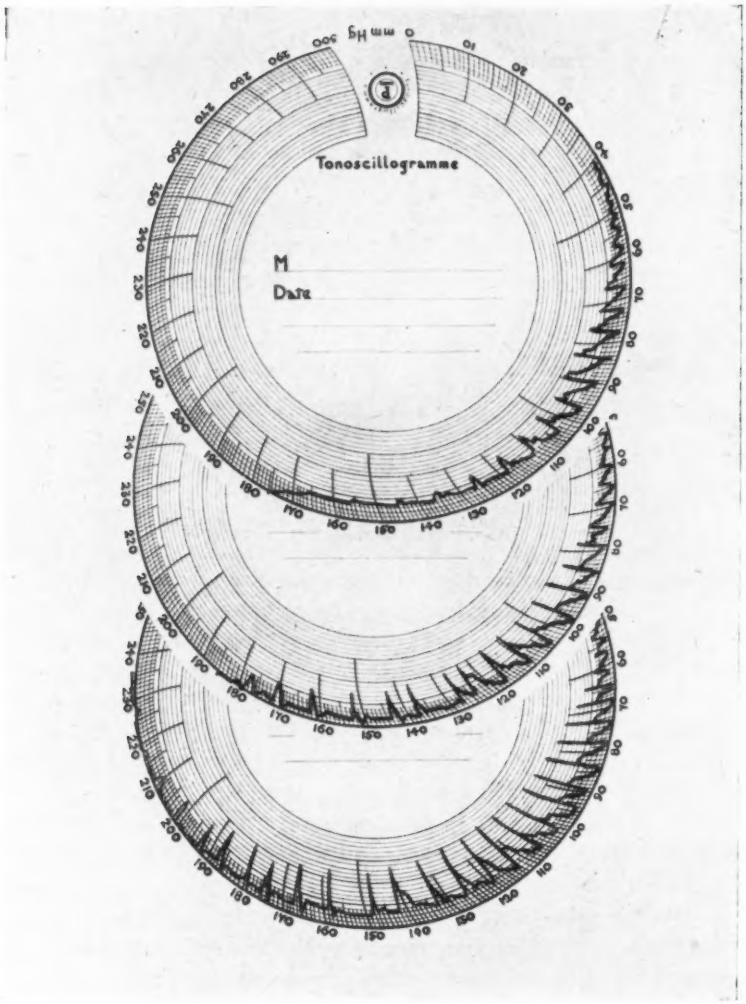
particularly the cardiovascular system, will depend on at least two factors: (i) The duration of the bout; (ii) whether the bout consists of a number of forced expirations alternating with a number of inspirations, or whether inspiration is slight or almost completely absent until the paroxysm is finished.

If inspirations interrupt the expiratory efforts then the effects on the circulation are to some extent being neutralized and little adverse effect usually results. If, however, there are a number of expiratory efforts, possibly associated with the valve-like effect of a certain type of glottic spasm, with little or no inspiratory interruptions, then the effects on the circulation may well be considerable. It is probably this type of paroxysmal coughing, seen best in whooping-cough, that is usually associated with attacks of loss of consciousness. It was this type of coughing that was present in the cases reported here. Unfortunately in other reported cases the cough is usually not described except as slight or severe.

In the paroxysmal cough the air is forced through the glottis by a series of expiratory efforts, with little or no inspiratory interruptions, so that at the end of the spasm the blood passing through the lungs has been most imperfectly oxygenated. The fixing of the chest by the spasm and the rise of pressure within the thorax effectively prevents the proper return of blood to the great veins, in particular the vessels of the head and neck become greatly congested as shown by the suffusion and cyanotic colour of the face, while the intra-auricular pressure rises steeply and sharply (McMichael, 1946). At the same time the blood-pressure is elevated and may rise to considerable heights (*see* fig., page 144).

When considering the effects of this type of coughing it is essential first of all to be certain that acute cerebral congestion, uncomplicated by other factors, can on occasion cause loss of consciousness.

Cerebral congestion is far less common and is less well understood than is cerebral anæmia which may often occur as a separate entity and which is more easily produced experimentally. The relationship of cerebral congestion to unconsciousness is more obscure. Congestion such as may be produced by constricting the neck, under certain conditions, inevitably causes loss of consciousness. Unfortunately at the same time there are complicating factors which may of themselves produce unconsciousness such as obstruction of the airway, carotid sinus syncope or reflex effects from the pharynx or larynx, so that it is difficult to separate the various factors. Obstruction to venous return by tumours or similar slowly acting mechanisms are not comparable to the conditions produced by coughing



To show the effect of coughing on the systolic blood-pressure of a young male adult.

Chart 1 is a control oscillogram taken in the sitting position. The systolic pressure is 118 and the size of the maximum excursion is just under 0·9 cm.

Chart 2 taken in the sitting position immediately after a bout of voluntary coughing lasting 30 seconds. In this bout of coughing after each second or third expiratory effort there was an inspiration. The systolic pressure is 178 and the size of the maximum excursion is 1·0 cm.

Chart 3 taken in the sitting position immediately after a voluntary bout of paroxysmal coughing lasting about 12 seconds. In this bout of coughing there were expiratory efforts only with no intervening inspiration.

The systolic pressure is 202 and the size of the maximum excursion is 1·3 cm.

for they lack that element of suddenness which is such an essential factor in producing loss of consciousness from many causes. The brain dislikes sudden changes whether due to anæmia or congestion, sudden alterations in pressure or sudden changes in oxygen tension and is apt to react to such changes, which may be quite opposite in character, by causing loss of consciousness.

In the consideration of the effects of congestion on the mental processes help may be obtained from aviation medicine. Probably the purest type of cerebral congestion is that caused by one form of centrifugal effect —negative acceleration—which is sometimes produced by flying. This effect is seen during outside loops and rolls when the centrifugal effect is from the legs and abdomen towards the head. This is far less common than the positive acceleration when the blood is driven from the head to the abdomen and legs in the usual turn at high speed or the inside loop. Most of the experimental work on negative acceleration has been done in giant centrifuges with human beings as subjects or with animals (Armstrong, 1939). It is more dangerous than positive acceleration, for permanent injury may result from intracranial hæmorrhages. During negative acceleration the forces acting on the circulatory system increase the arterial flow to the brain and obstruct the venous return, causing congestion within the cranium. As a result of these stresses unconsciousness has been caused in experimental animals but no case of unconsciousness in man has been reported. At comparatively slight negative accelerations the subject feels dazed and confused and there may be neuromuscular inco-ordination. This mental upset may last some minutes and is followed by a period of mental confusion.

This type of congestion differs, however, from that occurring as the result of paroxysmal coughing. There is no marked increase in intrathoracic pressure unless, as may happen, the subject reacts to the stress by ceasing to breathe and tensing the musculature of the thorax. There is thus no obstruction to the venous flow from the abdomen and lower limbs, on the contrary the centrifugal force tends to force the venous blood back to the heart while decreasing the arterial flow, although to a lesser extent.

A state of affairs more comparable to that found in paroxysmal coughing occurs during the performance of the 40 mm. of mercury test originated by Martin Flack, which has been a routine test in the Royal Air Force for many years. In this test the candidate blows a column of mercury contained in a U tube to a height of 40 mm. and holds it there for as long as possible. The average healthy young adult will keep the mercury up to

the required height for 50 to 60 seconds, while some will keep it up for 100 seconds or more. During the test the intrathoracic pressure rises from the normal −1 to −4 mm. of mercury to about +18 to +25 mm. This pressure causes considerable obstruction to the venous return and the exact means by which the circulation can overcome the results of the increased intrathoracic pressure and reach a state of apparent temporary equilibrium are imperfectly understood. One of the first effects is obstruction to the return flow of blood from the great veins partly because the intravenous pressure is now below the intrathoracic pressure level, partly because of withdrawal of the pumping action of respiration. In consequence there is a diminution of the return to the heart with a resultant lessening in the size of the pulse. What return flow there is to the heart depends largely on the difference between intra-abdominal and intrathoracic pressure. If the abdominal muscles are firm and good the intra-abdominal pressure is the greater thus ensuring a continuous, if reduced, return via the inferior vena cava (Warner *et al.*, 1925). It is probably as a result of this, combined with some return flow from the head veins, that allows the heart to continue working at a reduced level which is usually sufficient to keep the cerebral circulation functioning satisfactorily. In a normal healthy young man the pulse diminishes in volume while the rate taken at 5-second intervals varies hardly at all. On the other hand the blood-pressure in practically every case shows a rise which differs greatly in different individuals. This rise may begin almost immediately, or may not begin till the test has been in progress 30 seconds or more. The greatest height occurs about the time the subject gives up or just after, when he has taken his first deep inspiration after letting the mercury drop. In a series of blood-pressure readings in 60 individuals while doing the test a rise of 40 to 60 mm. of mercury was common. In one instance the blood-pressure rose from 140 to over 250 mm. of mercury and in 12 others the rise was to over 200 mm. In other instances the increase amounted only to a few millimetres and it was impossible to foresee which subject would show a big rise and which a small one. These circulatory changes are closely comparable to those which occur in paroxysmal coughing. Many thousands of these tests have been done in the R.A.F. and it is not unknown for a subject, who is particularly anxious to excel at his medical tests, to carry on till consciousness is lost and twitching movements of the limbs have occurred. It must be stressed that this nearly always occurs when forced expiration has lasted for over a minute and is rarely seen in those who give up after shorter periods. This effect is analogous to that seen during the tug-of-war when fixation of the thorax adversely affects

the respiratory and circulatory systems causing collapse or fainting (Hambly *et al.*, 1922).

What causes the loss of consciousness is unknown; it may be anoxia or it may be the results of the pressure changes within the cranium. It is likely that the circulatory system of different individuals reacts differently to the strain caused by paroxysmal coughing. The duration of the paroxysm, the degree of anoxia and the rapidity with which it is produced, the completeness or incompleteness of the valvular action of the glottis will all affect the outcome and it may well be that two or more factors must be coincident for an attack of unconsciousness to occur. It is therefore not surprising that attempts to reproduce the symptoms by voluntary coughing or by such methods as attempting to obstruct the venous return from the head do not meet with success.

There can be no doubt that cerebral congestion can cause unconsciousness even if the mechanism by which it does so is obscure. Paroxysmal coughing, under certain circumstances in certain individuals, causes cerebral congestion which apparently may be severe. There seems no reason to postulate in every instance an epileptic basis for these attacks of unconsciousness, in fact it is probably the exception rather than the rule.

Conclusion.

It seems probable that the syndrome in which loss of consciousness associated with coughing are the predominant symptoms has no single basis of causation. True vertigo is rarely, if ever, present and the name "laryngeal vertigo" should not be used.

Some cases are epileptic in origin but there is evidence that a majority may result from the circulatory changes induced by the cough. A diagnosis of epilepsy should only be made when other evidence points to the patient being an epileptic. Unless there are clear indications, as shown for instance by the tendency to recurrence and the occurrence of attacks unassociated with coughing, or when the E.E.G. points to epilepsy, the basis of attacks should be regarded as cardiovascular in origin.

Summary.

(1) Three cases of unconsciousness associated with coughing are reported.

(2) The theories of the causation of these attacks are discussed and reasons given why it is believed that a majority of the cases are the result of altered cardiovascular conditions due to the paroxysms of coughing.

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THE EFFECT OF RUPTURE OF THE PERINEURIUM ON THE CONTAINED NERVE-FIBRES.[1]

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The observations which form the subject of this paper concern the behaviour of nerve-fibres contained within a funiculus when the tubular protecting sheath of perineurium is ruptured.

Dustin (1918) claims to have demonstrated (1917—not available for reference in this country) that when the perineurium is ruptured the funiculus undergoes serious changes which affect all the contained fibres. He described the degeneration of axons, demyelination, the exuberant development of a glioneuroma invading neighbouring tissues and creating extensive adhesions and finally the invasion of the ruptured bundle by connective tissue. As a result "très rapidement, toutes les fibres nerveuses contenues dans le fascicule dont la gaine lamelleuse a été rompue, sont frappées d'incapacité fonctionelle." It is not clear from his account whether Dustin believed that the involvement of fibres topographically remote from the site of rupture was due to the causative injury or was a secondary consequence of rupture of the perineurium. It would appear, however, that he inclined to the latter view since it was on that basis that he advanced the opinion that the consequences of a lateral injury (incomplete notching) in a poorly funiculated zone were more serious than those following the corresponding involvement of a richly funiculated zone. According to him a large bundle or bundles would be involved in the former and rupture of the perineurium would result in more extensive degeneration than in the latter where the injured bundles would be smaller and the nerve-fibres in them would comprise only a few of those composing the nerve. Proceeding on this assumption he argued that a lateral neuroma in a richly funiculated zone should be discretely excised and partial suture performed whereas such a neuroma in a poorly funiculated zone should be fully resected and complete suture performed.

An indirect reference to this subject is contained in a recent paper on the effects of experimental percussion of the sciatic nerve in the cat

[1] Financial assistance from the National Health and Medical Research Council is gratefully acknowledged.

(Denny Brown and Brenner, 1944). In some experiments percussion resulted in rupture of the perineurium. When this occurred "Myelinated fibres with irregular neurofibrillar regeneration bulged through the opening. . . . The myelin in the remainder of the bundles was swollen and irregular on all fibres. Demyelination, leaving naked axis cylinders, was present in scattered fibres throughout the unherniated portion. . . ." The resulting hernia was described as being "associated with great disorder of conduction of sensation and movement in some fibres for longer than six weeks, which is longer than the usual duration of paralysis from severe uncomplicated percussion at the midsciatic level." This was followed by the observation that "even when the hernia is single and small the remainder of the nerve-fibres in the nerve show the patchy demyelination characteristic of percussion lesion, with corresponding partial or complete block." Whether these changes were attributed to the rupture or to the blow is not stated.

The experiments to be described were planned to determine the intrafunicular consequences of rupture of the perineurium brought about by a traumatic injury which was so sharply localized on the surface of a large bundle as to involve directly only the subjacent fibres. In this way it was hoped to establish whether rupture of the sheath alone is sufficient to precipitate total or widespread degenerative changes within the funiculus.

Material and Methods.

Under chloroform anæsthesia and aseptic conditions the left ulnar nerve of the common Australian opossum (*Trichosurus vulpecula*) was exposed above the medial humeral epicondyle where it is composed of a single large bundle with, occasionally, one or two small satellites. The perineurium of one quadrant of the large bundle was neatly incised with fine, sharp scissors following which a small herniation developed. The wound was then closed. This operation was repeated in 10 specimens though the depth of the incision varied slightly at each operation. The nerve was re-exposed at intervals varying from ten to twenty-one days. After observing the effects of electrical stimulation above and below the site of rupture, where a small adherent glioneuroma had formed, the injured area, together with a length of the nerve proximal and distal to it, was removed and placed in 10 per cent. formalin. The excised segment was then treated by Swank and Davenport's (1935) method for demonstrating degenerated nerve-fibres. The material was embedded and serial sections cut at 15 μ—these were counterstained with van Gieson. In some specimens the nerve was sectioned transversely and in others longitudinally.

Observations.

Information relating to the behaviour of the nerve-fibres contained in the ruptured bundle was provided by:

(1) *Post-operative observation of the affected hand.*—The hand and digits of the opossum are capable of a wide range of movements. Those required in climbing and feeding, which involve ulnar-supplied muscles, were not impaired so far as could be ascertained by observation.

(2) *Inspection of the site of injury at the second operation.*—Exploration of the nerve revealed at the site of injury a small irregular lateral mass which, though adherent to the surrounding tissues, could be easily separated from them by gentle dissection. The appearance of the mass suggested that it was composed of herniated intrafunicular contents—histological examination showed it to be an organizing glioneuroma. Nerve-fibres which appeared to be normal were observed coursing past the glioneuroma.

(3) *Electrical stimulation of the exposed nerve proximal and distal to the site of rupture.*—Localized stimulation of the nerve above, at, and below the site of the injury, produced contraction of the flexor carpi ulnaris and digital movements consistent with contraction of some, at least, of the intrinsic muscles of the hand supplied by the ulnar nerve. These responses were obtained in specimens in which the nerve was composed of a single bundle only thereby indicating that uninjured satellite funiculi could not have been responsible for the transmission of the impulses.

(4) *Observation of the reflex responses elicited during the removal of the nerve segment for histological examination.*—Widespread reflex responses were produced during the division of the nerve below the site of rupture—these were abolished by severing the nerve proximal to the injured zone prior to, or during, its division distally. This indicated that impulses had travelled centrally past the site of damage. For reasons set out in Section 3 these impulses could not, in some specimens, have been transmitted by intact satellite bundles.

(5) *Histological examination of the excised segment.*—The extent of the Wallerian degeneration and the nature of the tissue reaction were, in each case, related to and dependent on the depth of the incision and duration of the experiment. In each specimen the fibres showing degenerative changes were those directly involved at the site of rupture. Fig. 1a, which is of a transverse section of the nerve, illustrates the condition obtaining at the site of injury in that specimen eleven days after the operation. Fig. 1*b* illustrates the number and distribution of the fibres showing Wallerian degeneration, which represent only a proportion of

those comprising the bundle, distal to the site of injury in the same nerve. The scattering of some of the degenerated fibres is due to the intrafunicular shift of nerve-fibres which occurs as a part of the process of intraneural funicular plexus formations.

The nature of the glioneuromatous and connective tissue reaction at the site of rupture suggested that the direction of the reaction was from within outwards. For the duration of the present experiments there was no tendency for the extrafunicular connective tissue to invade the funiculus but rather for the contents of the latter to force their way externally. Experiments of longer duration are in progress.

Conclusions.

The results of the present investigation demonstrate that rupture of the perineurium does not itself lead to total or even widespread degeneration within the bundle. The only fibres showing degenerative changes in these experiments were those damaged at the site of rupture. Though the findings did not completely exclude the possibility that some of this subtotal involvement might have been consequential on the breach they favoured the interpretation that all the affected fibres were damaged at the time of the original injury by the agent causing the breach. Thus where widespread or total intrafunicular degeneration occurs in association with rupture of the perineurium the former should be attributed directly to the causative injury or to influences (other than rupture of the perineurium) introduced by it. It was not possible to ascertain whether rupture of the perineurium alone, so that the underlying fibres remained undamaged, would result in any degeneration of the subjacent fibres or whether it would be followed by their herniation through the rent with subsequent changes leading to degeneration. In any case a rupture of this restricted type would be a rare event in traumatic injuries.

In the light of these findings Dustin's original thesis, relating to the consequences of lateral injury to richly and poorly funiculated zones respectively of a peripheral nerve, requires revision.

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LEGENDS FOR FIGURES.

Fig. 1.—Photomicrographs of transverse sections of the ulnar nerve (specimen 5) taken at (*a*), and below (*b*), the site of rupture eleven days after the injury. (*a*) ×45; (*b*) ×60.

PLATE XIV.

FIG. 1A.

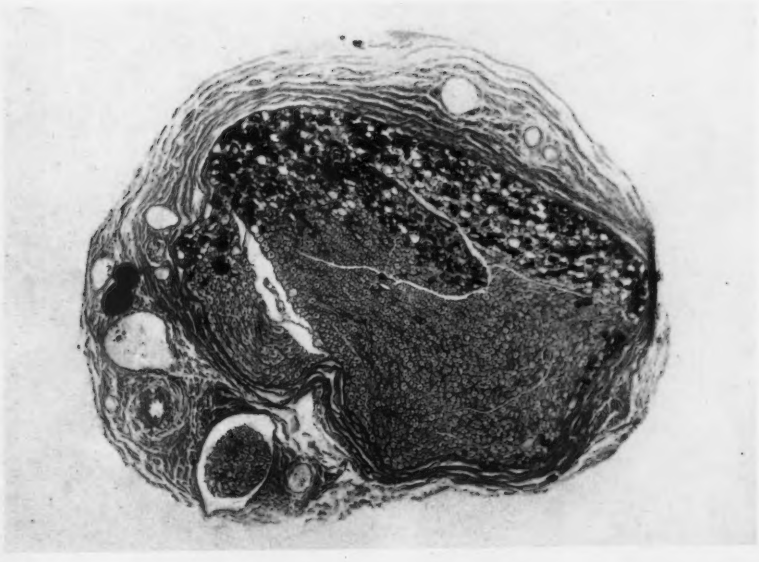

FIG. 1B.

To illustrate article by Sydney Sunderland

Notices of Recent Publications.

Les gliomes infiltrés du tronc cerebral. Par G. Guillain. I. Bertrand et Jean Gruner. Paris. Masson et Cie. 1945. Pp. 286. Figs. 119. (Price not stated.)

This monograph fills a gap left by the numerous American monographs on different types of brain tumour. While it follows the general lines adopted in these books, it is more detailed and complete than most of them. Full case-histories, well worked out both on the clinical and pathological sides, are given of twelve cases of diffuse glioma of the brain-stem. Most of these represent the common type of glioma pontis, with extensions in some either upwards to the thalamus or downwards into the medulla. A case of tumour of the left thalamus and mid-brain, and a remarkable case in which the tumour extended from the vertex of the frontal lobe to the medulla, are also included. One of the pontine gliomas had produced widespread meningeal infiltration.

In the historical introduction it is surprising to find it stated that the condition is still regarded as a rarity in the United States although it is reported to have occurred in from 3 per cent. to 15 per cent. of all intracerebral tumours in statistics from that country; the larger percentages have been observed in pediatric clinics. It is almost equally surprising to find that a large proportion of American cases have been wrongly diagnosed as encephalitis.

The authors discuss in a comprehensive manner the symptomatology and pathology of these tumours, indicating the great variations in clinical signs and in pathological type. Only one page is devoted to treatment, but this may be adequate for tumours with so hopeless a prognosis.

The volume is beautifully illustrated by photographs and diagrams and altogether conforms to the high standard that we have learned to expect from its senior authors. There is a full bibliography but no index.

Agnosia, Apraxia, Aphasia. Their value in Cerebral Localization. By J. M. Nielsen. Second Edition, completely revised. P. B. Hoeber, Inc., New York and London. 1946. 59 Illustrations. Pp. 292. Price $5.00.

The application of disordered speech as a localizing symptom in neurological disease has tended to become a dated, if not discredited, practice. Here is an attempt to rescue this aspect of aphasia from discard. The author has made good use of his opportunities of studying and following up a large series of arteriopaths. Turning to the massive though neglected monograph of Henschen, all case material with adequate post-mortem verification has been scrutinized, classified and brought up to

date. Recent neurosurgical activities have played their humble part in assisting the problem, by adding their quota of lobectomies and even—be it said—ablations of complete hemispheres. Professor Nielsen has staunchly followed Hughlings Jackson in assigning to the right half of the brain a not inconsiderable function in speech. Indeed, throughout this monograph discrimination is made between the role of the dominant and recessive halves, or as the author would prefer to call them, the major and minor hemispheres. Some important conclusions are proffered from the collected pathological material. The minor hemisphere can assume the function of the major with varying degrees of facility. If the language function is partly destroyed it does not usually transfer to the minor hemisphere completely; but the motor, visual, or auditory components may go separately. An artificial writing mechanism may be formed on the minor side by training; when this happens the entire speech mechanism does not of necessity move to the minor side (thus supplying an answer to the question put down years ago by Gowers). But, in the author's opinion, the major temporal lobe and the major occipital lobe may not be ipsilateral. The author is forced to conclude that it is unsafe to lateralize a cerebral lesion merely upon the basis of an aphasia.

Many new terms appear in this monograph, as well as novel classical classifications. "Eugnosia" and "Euphasia" are newcomers. A "formulation aphasia," associated with disease of Brodmann's area 37, is described. "Irreminiscence" is put forward to indicate loss of recall, qualified as required by various descriptive adjectives.

There is a useful chapter dealing with the body scheme and its disorders and the author makes an interesting distinction between disturbances of the "anatomic" and of the "physiologic" body scheme, the former relating to lack of recognition of the existence of parts of the body (positive or negative) and the latter to lack of insight into disordered function of various limbs or organs. We recognize the autotopagnosias in the one and the anosagnosias (or Anton's symptom) in the other.

A stimulating and laudable addition to the literature of aphasia is the result. The method of approach may not be approved by the dynamist school of neuropsychology, but it is not the less useful for all that.

Motor Disorders in Nervous Diseases. By E. Herz and Tracy Putnam. King's Crown Press, New York. 1946. Pp. 184. Price £1.

It appears that this clinical guide was designed to be read in connection with a series of films illustrative of the main forms of motor disorder. It contains chapters descriptive of all modes of incoordination and of abnormal reflex reactions in the limbs and trunk, and also special chapters devoted to cranial nerve palsies. It is richly illustrated by "still" photographs and by short series taken from cinema films.

It is a curious mixture of the rudimentary and of the advanced. Thus, pictures illustrate the modes of eliciting the various tendon-jerks, and brief text descriptions accompany each picture. On the other hand we read numerous statements like the following. "Brain stem mechanisms subserve management of associated and synergising movements definitely necessary to maintain complete coordination. They regulate initiation and perseverance of simple movements and compound acts, they are important in maintaining postures by the insertion of associated movements and are responsible for the correct distribution of automatic movements which accompany every motor act and appear spontaneously as expressive or affective accompanying movements."

Fifty years ago the great teachers of clinical medicine did not write like this, and it is not unfair to say of the paragraph quoted that it embodies no clear ideas and conveys no information. The authors express the hope that their book will fill an empty place in the teaching of neurology, but surely clinicians are not trained in this fashion, but only by the direct observation and handling of the material of their study—the patient—aided by clearly and simply written texts.

Autonomic Regulations. By E. GELLHORN. Interscience Publishers Inc., New York. 1943. Pp. 373. Price $5.50.

This closely written work concerns itself with the role of the autonomic system in the integration of the internal environment of the organism. Those organs which are influenced by the autonomic system and affect it in turn are subjected to a physiological analysis. The mutual relations of hormones and autonomic system, and of somatic and autonomic nervous systems are considered.

Every aspect of autonomic function is covered and a clear and complete account provided by the author. There is a bibliography of over a thousand papers.

The author is to be congratulated on a comprehensive work of reference that will probably become the standard in its particular field.

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